Cochlear Implants International

# Cochlear implant outcomes in patients with Meniere's disease: a large case series

--Manuscript Draft--

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| **Abstract:** | Objective: To perform a matched cohort study to assess whether patient's with Meniere's Disease (MD) require more intensive auditory rehabilitation following cochlear implantation and identify factor(s) that may affect outcomes in patients with MD.<br>Methods: A retrospective case review was performed using electronic/paper records and departmental database. All MD and control patients were matched for age, biological sex, implant manufacturer and electrode design. variables measured include: age at implantation, duration of deafness pre-implantation, pre- and post-operative MD state (whether active MD+ or inactive MD-), laterality of implantation relative to disease side, pre- and post- operative ablation treatment and electrode design. Outcomes measured were speech scores, number of visits to audiology department following switch-on and post-operative progression to active MD.<br>Results: Forty consecutive implanted MD patients were identified between May 1993 and May 2019. Although post-operative speech scores in MD patients were comparable to those within the control group, patients with active MD following implantation required significantly more visits to the audiology department compared to |

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|---|---|
| | controls (p<0.01) and patients who had inactive mD post-operatively (p<0.01). However, in MD patients, active MD was less likely following CI surgery (p=0.03). This is because fifty-five percent of patients with pre-operative active MD ceased to experience active MD post-operatively., while none of the patients with inactive MD prior to implantation progressed to active MD post-operatively. In those who continued to experience active MD post-operatively, further medical and surgical ablative intervention was required to control ongoing menieres attacks.<br>Conclusion: We present the largest case series of performance outcomes in CO patients with MD. Although speech outcomes in MD patients are comparable to controls, patients with active MD pre-operatively are more likely to experience variation in CI performance requiring a prolonged period of auditory rehabilitation compared to inactive pre-operative MD. |
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| **Response to Reviewers:** | Thank you for your comments. I addressed the minor issues outlined below.<br><br>Kind regards,<br><br>1. Please specify if you mean biological sex or gender in the participant section.<br>-I have amended this to biological sex<br><br>2. Please include outcomes of the comparison of MD+ and the control group for the speech recognition outcomes.<br>Under the section 'Speech comprehension outcomes do not depend on post-operative MD status' I have clarified this area further.<br>-There were also no significant differences between either the MD+ group and controls or the MD- group and controls (p>0.05; Wilcoxon signed-rank tests). Consistent with this, the improvement in speech scores following implantation was also similar for different patient groups (Figure 3b; no significant differences between groups; p>0.05), albeit slightly higher for the MD patients (particularly MD- patients). Consequently, when we compared the improvement in speech scores across groups, there was no significant difference between the MD+ and MD- groups (Mann-Whitney U test; p>0.05), and there were no significant differences between either the MD+ group and controls or the MD- group and controls (Wilcoxon signed-rank tests; p>0.05).<br>- |

Table

| | **MD patients** ***n=40*** | **Controls** ***n=40*** |
|---|---|---|
| Age at implantation (years), median [interquartile range] | 62 [46-70] | 58 [42-70] |
| Sex, No (%) | | |
| Female | 18 (45.0%) | 19 (47.5%) |
| Male | 22 (55.0%) | 21 (52.5%) |
| Implant manufacturer, No (%) | | |
| Cochlear | 18 (45.0%) | 18 (45.0%) |
| Advanced Bionics | 10 (25.0%) | 10 (25.0%) |
| Med-El | 12 (30.0%) | 12 (30.0%) |
| Implant model, No (%) | | |
| Pre-curved array | 6 (15.0%) | 6 (15.0%) |
| Lateral wall array | 34 (85.0%) | 34 (85.0%) |

**Table 1**. Comparison of patient characteristics and demographics between the Meniere's Disease (MD) and control groups. Median age at implantation (and interquartile range) is shown for each patient group. Other characteristics are summarized by the numbers (and percentages) of patients exhibiting each characteristic. Each MD patient was paired with a control that was matched for gender (with one exception) and age. Implant model and manufacturer were precisely matched between groups.

| Domain | *n* | Breakdown |
|---|---|---|
| **MD Laterality** | 40 | Unilateral (21)<br>Bilateral (19) |
| **Side of Implantation** | 40 | Ipsilateral to MD ear (35)<br>Contralateral to MD ear (5) |
| **Additional Aetiology of Hearing Loss** | 14 | Congenital rubella (3)<br>Meningitis (2)<br>Noise exposure (2)<br>Congenital idiopathic (1)<br>Otosclerosis (1)<br>Kernicterus (1)<br>Measles (1)<br>Iatrogenic profound SNHL (2)<br>Sudden onset SNHL (1) |
| **Past Medical History Relevant to Balance** | 25 | Visual impairment (4)<br>Severe MSK disease (2)<br>Superior semi-circular canal dehiscence (1)<br>Vestibular migraine (2)<br>Vestibular migraine and severe MSK disease (1) |
| **Balance Problems** | 19 | Bilateral hypofunction (10)<br>Unilateral hypofunction (9) |
| **Electrode Array Type** | 40 | Lateral wall array (34)<br>Pre-curved array (6) |
| **Pre-CI Surgical Ablation** | 24 | CN 8 section and right vestibular nerve section (1)<br>Labyrinthectomy (1) |
| **Complications** | 8 | BPPV (3)<br>Soft failure (2)<br>Hard failure (1)<br>Re-implantation (1)<br>Non-auditory stimulation following temporal bone fracture (1) |

**Table 2**. Additional characteristics of Meniere's Disease (MD) patients that were not related to either numbers of audiological visits, speech scores (pre- or post-operative), or progression to active MD following cochlear implantation (CI; $p > 0.05$ in all cases). [Abbreviations: BPPV: Benign paroxysmal positional vertigo; CN: cranial nerve; MD; MSK: musculoskeletal; SNHL: Sensorineural hearing loss].

| Patient | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| **Side of disease** | B/L | B/L | Left | Left | B/L |
| **Side implanted** | Right | Right | B/L (sequential) | Right | Right |
| **Balance testing** | B/L hypofunction, > on left side | Calorics abandoned | Left hypofunction | Left hypofunction | B/L hypofunction, equal on both sides |
| **Reason for implantation to contralateral MD ear** | MD burn out > 30 years ago in the ipsilateral side | Active MD on contralateral side at time of implant. | Soft failure on ipsilateral side therefore contralateral side implanted | Dead ear on ipsilateral side from previous stapes surgery > 20 years ago. | MD burn out in the ipsilateral side, worse hearing in the contralateral ear |
| **Pre-operative MD state** | MD- | MD+ | MD+ | MD+ | MD- |
| **Post-operative MD state** | MD- | MD+ on C/L side | MD+ | MD+ | MD- |

**Table 3**. Rationale and outcomes for implantation contralateral to the diseased ear in Meniere's Disease (MD) patients. Although many MD patients experienced MD bilaterally (B/L; n=19, 47.5% of the total), a slightly greater number of MD patients experienced MD unilaterally (n=21; 52.5% of the total). In unilateral MD patients, the ear ipsilateral to the MD was implanted where possible (n = 35; 87.5% of the total). However, in a minority of MD patients (n=5; 12.5% of the total), it was necessary to implant the side contralateral (C/L) to the MD ear. For each of these patients, the reasons for this are described. As noted above, implantation did not change whether these patients' MD was either active (MD+) or inactive (MD).

Figure

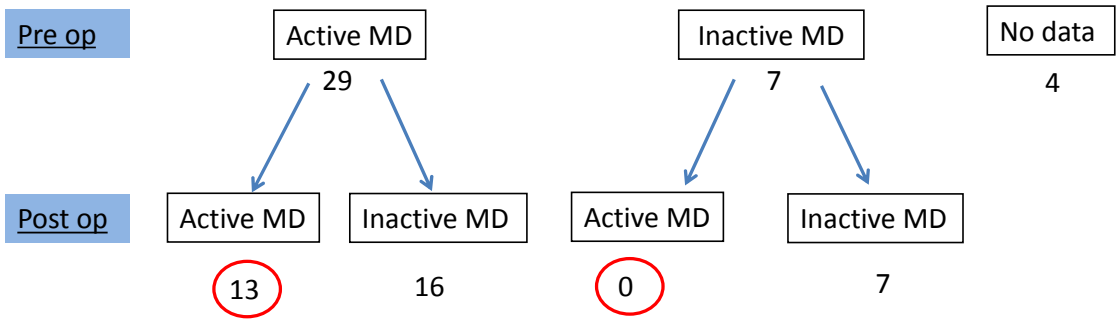


**Figure 1.** Prevalence of active Meniere's Disease (MD) before (pre-op) and after (post-op) cochlear implantation (CI). Data are shown separately for MD patients who experienced active or inactive MD before implantation. Overall, the prevalence of active MD was reduced following CI.

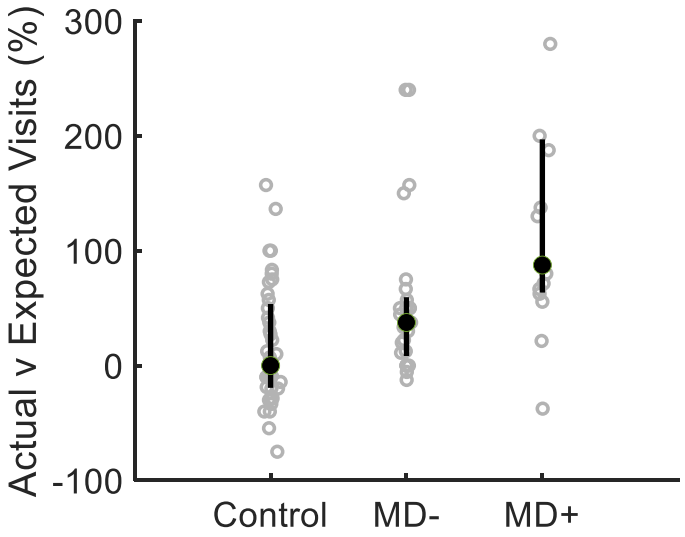


**Figure 2.** Differences between actual and expected audiological visits for different patient groups. Data are shown for patients who do not have Meniere's disease (Control) as well as patients whose Meniere's disease was either active (MD+) or inactive (MD-) following cochlear implantation. Medians (±interquartile range) for each patient group are shown in black, with individual patients denoted by grey symbols. Patients visited audiological services either more frequently than expected (positive values) or less frequently than expected (negative values), with values of 0 indicating patients whose visits perfectly matched expectations. Expectations were based on those typically seen in cochlear implant patients in our clinic.

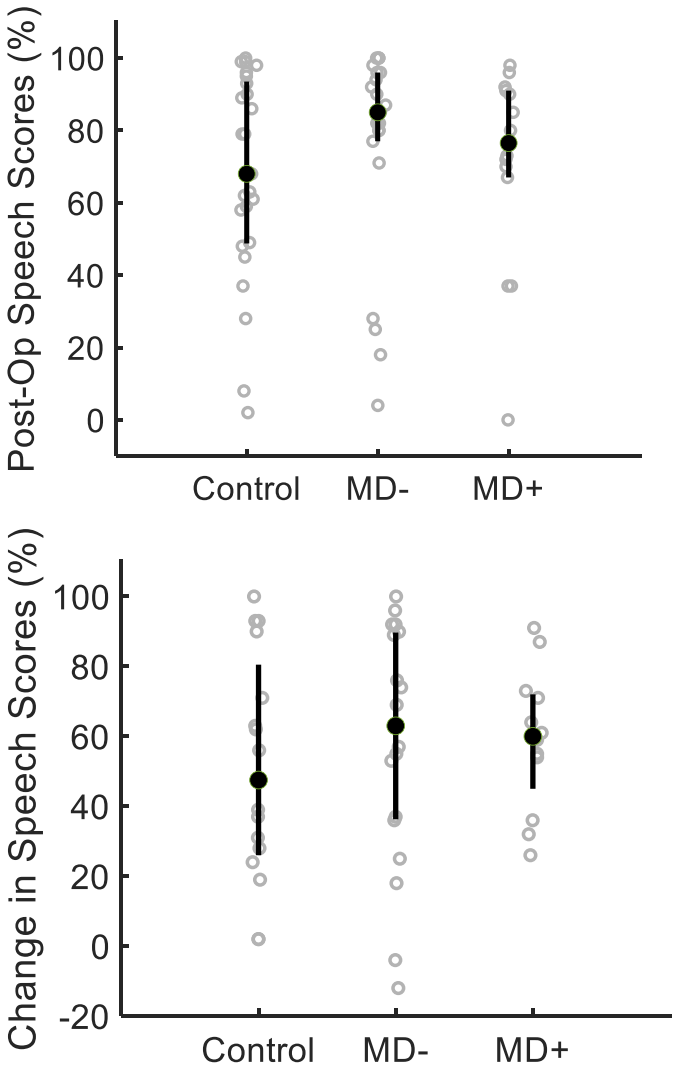


**Figure 3.** Speech comprehension outcomes in MD patients and controls. **A** Post-operative speech scores for different patient groups. Data are shown for patients who do not have Meniere's disease (Control) as well as patients whose Meniere's disease was either active (MD+) or inactive (MD-) following cochlear implantation. Medians (±interquartile range) for each patient group are shown in black, with individual patients denoted by grey symbols. **B** Differences between pre- and post-operative speech scores for different patient groups. All plotting conventions are identical to A. Cochlear implantation improved speech scores for the vast majority of patients (positive values) but led to slightly worse speech scores (negative values) in two MD- patients.

**Title Page**

# Cochlear implant outcomes in patients with Meniere's disease: a large case series

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**ABSTRACT**

*Objective:* To perform a matched cohort study to assess whether patients with Meniere's Disease (MD) require more intensive auditory rehabilitation following cochlear implantation and identify factors(s) that may affect outcomes in patients with MD.

*Methods:* A retrospective case review was performed using electronic/paper records and departmental database. All MD and control patients were matched for age, biological sex, implant manufacturer and electrode design. Variables measured include: age at implantation, duration of deafness pre-implantation, pre- and post-operative MD state (whether 'active' MD+ or 'inactive' MD-), laterality of implantation relative to disease side, pre- and post-operative ablative treatment, and electrode design. Outcomes measured were speech scores, number of visits to audiology department following switch-on, and post-operative progression to active MD.

*Results:* Forty consecutive implanted MD patients were identified between May 1993 and May 2019. Although post-operative speech scores in MD patients were comparable to those within the control group, patients with active MD following implantation required significantly more visits to the audiology department compared to both controls ($p<0.01$) and patients who had inactive MD post-operatively ($p<0.01$). However, in MD patients, active MD was less likely following CI surgery ($p=0.03$). This is because fifty-five percent of patients with pre-operative active Meniere's disease ceased to experience active Meniere's disease post-operatively, while none of the patients with inactive MD prior to implantation progressed to active Meniere's disease post-operatively. In those patients who continued to

experience active MD post-operatively, further medical and surgical ablative intervention was required to control ongoing Meniere's attacks.

*Conclusion:* We present the largest case series of performance outcomes in CI patients with MD. Although speech outcomes in MD patients are comparable to controls, patients with active MD pre-operatively are more likely to experience variation in CI performance requiring a prolonged period of auditory rehabilitation compared to inactive pre-operative MD.

*Keywords:* Meniere's disease, cochlear implantation, impedances, hospital visits, speech scores

## INTRODUCTION

Profound bilateral hearing loss may occur in patients with Meniere's Disease (MD) due to end stage disease or loss of hearing following ablation of the inner ear. Many studies have demonstrated that patients with MD undergoing cochlear implantation (CI) may develop comparable or above average auditory performance scores compared with non-MD patients. (Manrique-Huarte et al., 2018, Lustig et al., 2003; Mick et al., 2014 ) as well as improved tinnitus scores (Mick et al., 2014; Vermeire et al., 2014; Richardson et al., 2014). Following discussions with audiology colleagues both locally, and at national level within the British Cochlear Implant Group, it is widely recognised that this particular cohort of patients do present challenges with respect to post-operative programming due to ongoing distortions in auditory perception. Evidence based on small case series confirms high levels of auditory fluctuations which manifest as variations in cochlear implant performance (Holden et al., 2012; McNeill et al., 2016; Samy et al., 2016). High levels of impedance have also been noted in patients with active MD which has necessitated adjustments in implant mapping on a long term basis following initial rehabilitation (Holden et al., 2012; McNeill et al., 2016; Samy et al., 2016). This, in turn, may adversely impact quality of life and place greater demand on audiology-led services.

To confirm whether patients with Meniere's Disease (MD) require more intensive auditory rehabilitation and identify factors(s) that may contribute to variable cochlear implant performance in patients with MD. we performed a large retrospective review of all MD patients who underwent CI at our Institution.

## Methods

A retrospective review of all patients with MD undergoing cochlear implantation at a tertiary referral centre in London was conducted. Information was retrieved from Bawtry Computer Systems (BCS) database, electronic health records (EPIC Systems Corporation) and paper records. A control group of non-MD patients undergoing CI was included to evaluate any difference in outcomes between the two groups. In order to minimise any confounding effect, all patients in the control group were matched for age, biological sex (with one exception), implant manufacturer, electrode design and age at implantation with those in the MD group (ratio 1:1). Electrode arrays were classified as "straight/lateral wall" (LW) or "pre-curved/modiolar hugging"(MH). All cochlear implant surgery was performed using an atraumatic approach to maximise audiometric and vestibular outcomes post operatively.

### *Inclusion criteria*

All patients with a diagnosis of MD consistent with the AAO-HNS 1995, 2015 or 2020 definition were included in the series (Basura et al., 2020). The latest version of this criteria summarises patients into 2 categories; 'Definite MD and Probable MD'. Patients were classified into the 'active' post-operative group (MD+) if they exhibited subjective auditory fluctuations (i.e. changes in cochlear implant performance) in the presence or absence of vertigo and tinnitus. All patients satisfied audiometric and speech thresholds in line with national guidance (National Institute of Clinical Excellence, NICE) prior to 2019 to be deemed suitable for CI.

*Data fields*

Variables assessed included: duration of deafness pre-implantation; pre and post-operative MD state (active MD+/inactive MD-); laterality of implantation relative to affected MD side; relevant past medical history (visual impairment, vestibular migraine, superior semi-circular canal dehiscence, severe musculoskeletal disease), causes of hearing loss (e.g. meningitis, rubella, measles etc.); balance testing; pre and post-operative ablative treatment; electrode design; post-operative complications; pre and post-operative speech scores; and number of visits to the audiology from the switch-on to latest follow up.

Speech scores were measured using Bamford-Kowal-Bench testing (BKBs) in quiet. The number of expected visits to audiology following implantation was calculated using the standard hospital protocol of 4-5 appointments within 3 months following implantation, then a yearly and 2 yearly review. The number of visits was presented as a percentage of 'normalised visits' using the following equation: 100 x (number of visits – number of expected visits)/number of expected visits. This means that when percentage of hospital visits is '0', it is aligned with the expected number of visits according to the hospital protocol. The number of visits was corrected for between the MD and control group based on time of implantation or transfer-in to hospital and the duration of follow-up

*Statistical analysis*

Statistical analysis was performed using two-tailed Chi-square tests, Mann Whitney U tests or Wilcoxon signed-rank tests, with Bonferroni correction used to correct for multiple comparisons.

## Results

Forty patients (18 females, 22 males) met the study inclusion criteria and were implanted between May 1993 and May 2019. The mean age at implantation was 62 years old (range: 26- 94 years) and mean follow up was 6.5 years (range: 6 months- 26 years). Table 1 compares the characteristics and demographics for MD and control groups.

### *Disease activity following cochlear implantation*

To assess the impact of cochlear implantation on MD symptoms, we investigated the prevalence of active MD post-operatively with that observed pre-operatively (Figure 1). In the pre-operative period, twenty-nine patients (72.5%) were MD+ compared with 7 (17.5%) MD- patients. Data on disease activity was unavailable for 4 patients (10%). Overall, we found that the prevalence of active MD was significantly reduced following CI surgery ($p=0.03$, chi-squared test). This is because 55% of the patients with active MD before implantation ceased to experience active MD post-operatively. In addition, none of the patients with inactive MD prior to implantation progressed to active MD post-operatively. A precise breakdown of these results (and the number of patients corresponding to each group) is illustrated in Figure 1. In patients who continued to experience active MD following CI (13/29; 45%), a minority (4/13; 31%) also required further treatment (including ablation) for active disease.

### *Number of post-operative visits to audiology depends on MD status*

To assess the audiological needs of MD patients following cochlear implantation, we next examined the number of post-operative visits to audiology for both MD+ and MD- patients. More specifically, we asked whether the number of visits to audiology was greater than that

expected for controls (Figure 2; see methods for details of how numbers of visits were normalized relative to expectations). We found that post-operative MD+ patients visited audiology departments more often than both post-operative MD- patients ($p<0.01$; Mann-Whitney U test) and controls ($p<0.01$; Wilcoxon signed-rank test). However, whilst post-operative MD- patients tended to visit audiology departments slightly more often than controls, this trend was not significant ($p>0.05$; Wilcoxon signed-rank test). In addition, no significant difference was found between MD patients with unilateral or bilateral MD (see Table 2 for a list of additional characteristics in MD patients that did not affect outcomes).

*Speech comprehension outcomes do not depend on post-operative MD status*

Since post-operative MD+ patients visit audiological services more often than controls, we next considered whether this might be because their speech comprehension outcomes are worse than either controls or MD- patients. However, whilst there was a slight trend for MD patients (particularly MD- patients) to do slightly better overall (Figure 3a), post-operative speech scores did not depend on MD status, with no significant difference between MD+ and MD- patients ($p>0.05$, Mann-Whitney U test). There were also no significant differences between either the MD+ group and controls or the MD- group and controls ($p>0.05$; Wilcoxon signed-rank tests). Consistent with this, the improvement in speech scores following implantation was also similar for different patient groups (Figure 3b; no significant differences between groups; $p>0.05$), albeit slightly higher for the MD patients (particularly MD- patients). Consequently, when we compared the improvement in speech scores across groups, there was no significant difference between the MD+ and MD- groups (Mann-Whitney U test; $p>0.05$), and there were no significant differences between either the MD+ group and controls or the MD- group and controls (Wilcoxon signed-rank tests; $p>0.05$).

*Disease laterality and side of implantation*

Thirty-seven patients underwent unilateral cochlear implantation and 3 underwent bilateral cochlear implantation. Reasons for bilateral implantation included visual impairment and soft failure on initial side. Five patients underwent cochlear implantation in the ear contralateral to the MD ear. The rationale for contralateral implantation was variable, including: disease burn out in the ipsilateral side, soft failure on the ipsilateral side necessitating sequential surgery on the active side, dead ear on the ipsilateral side and declining hearing in the contralateral ear. Three out of the 5 patients went on to have active disease. A more comprehensive breakdown of these findings is shown in Table 3. There was no significant difference in the number of post-operative visits between the ipsilaterally implanted group (n=35) and the contralaterally implanted group (n=5) (median visits 37.5 and 55.6 respectively, p=0.90, Mann Whitney test, see Table 2).

*Other Domains and complications*

Other variables assessed in the study made no significant difference to outcome and are outlined in Table 2.

**Discussion**

The aim of this study was to better understand how various factors shape CI outcomes in MD patients, using the largest case series of this type published to date. Following implantation, we measured the number of visits to audiology, speech comprehension outcomes, and the prevalence of active MD.

Our data clearly demonstrate that patients with post-operative MD+ required significantly more visits to the audiology department compared to controls. In the majority of instances,

the purpose of these visits was to troubleshoot distortions in auditory perception experienced by the patient which were thought to be related to ongoing active episodes of MD . In many cases this would require reprogramming of the device to improve the sound quality. Patients in the postoperative MD- group had slightly more visits than the controls, but these differences were not significant. It is therefore advisable that all MD patients are counselled that they are likely to require a prolonged period of rehabilitation following implantation. Although our results do not identify the reasons for this, previous studies suggest that patients with on-going fluctuations in hearing demonstrate increased impedances and ongoing mapping requirements (Samy et al., 2016). What is not clear is why these fluctuations arise. A possible explanation may be that the presence of intracochlear fibrosis following implantation may render the endolymphatic space more susceptible to hydrops (Fife et al., 2014; Lustig et al., 2003). Another possibility could be due to on-going vestibular dysfunction caused by autoimmune MD due to changes in vestibular physiology following implantation (Lesinski et al., 1998). Several reports in the literature describe increases in impedances during so called 'Meniere's attacks' (Holden et al., 2012; McNeill et al., 2016; Samy et al., 2016). One such study reports significantly larger impedances (>3 kohms) in the symptomatic MD side of a patient with bilateral cochlear implants (Samy et al., 2016). Over a 9-year follow up of this patient, only one episode of vertigo was experienced compared with multiple attacks of tinnitus during impedance increases, suggesting that changes in electrical stimulation are perceived by the auditory cortex (McNeill et al., 2016). The increases in impedance were found to consistently affect the more distal electrodes (9-16) which corresponded to the mid frequency range. The authors discovered that current recalibration within this range overcame the changes in impedance. The specific mapping strategies used to achieve this are unclear, and indeed our institutional experience has found that anecdotally some patients required an increased dynamic range, while others a reduction.

In our study, patients with MD tended to achieve higher post-operative speech scores when compared to controls. Even though this result seems to corroborate previous findings (Mick et al. 2014; Vermiere et al., 2014), this difference was found to be not statistically significant ($p=0.12$) in our analysis. Despite only 2 patients undergoing surgical ablation pre-operatively, this did not impact on post-operative speech scores when compared with matched controls, supporting the idea that ablative treatment prior to CI could be considered a reasonable option in this category of patients (Holden et al. 2012). In this regard, some authors suggest simultaneous labyrinthectomy with the aim to remove the environment where on-going disease can ensue (Foster et al., 2013; Lustig et al., 2003; Hansen et al., 2013; Doobe et al., 2015). In our case series, only one patient underwent endolymphatic decompression following CI and, therefore, conclusions on cochlear implant outcomes in this particular case could not be drawn. However, as a general rule, we advise to avoid any surgical treatment following CI as this may affect/alter the implant.

In this study, the prevalence of active MD was reduced following cochlear implantation. This was partly because no patients with inactive Meniere's disease preoperatively developed active Meniere's disease postoperatively suggesting CI surgery does not trigger activation of quiescent Meniere's disease. It would therefore appear that patients with pre-operative active disease are therefore most at risk of experiencing ongoing symptoms, however, it is possible that biochemical changes with the cochlear following implantation may potentially stimulate symptoms of MD in the pre-operative MD- group. The reduction in active MD prevalence following implantation was primarily because just over half (55%) of patients with active Meniere's disease preoperatively did not have active disease after cochlear implantation.

Nevertheless, forty-five percent of patients with pre-operative active Meniere's disease continued to have disease activity in the post-operative phase, with 4 of these patients requiring further treatment (including ablation) for active disease following implantation. All surgery was performed using an atraumatic approach in order to preserve audiometric and vestibular function.

We did not observe any significant differences between bilateral and unilateral CI in MD patients developing post-operative MD+ as additionally proven by our 10 patients who had confirmed pre-operative bilateral hypofunction. Although 3 out of 5 patients continued to have MD+ following implantation (Table 2), this difference was also not significant and had no impact on the number of post-operative visits to audiology.

By convention, the side of implantation will occur on the ipsilateral side of disease in order to preserve vestibular function in the contralateral ear which is assumed to have better vestibular function, Hence this should reduce the impact on balance in the post-operative period. For patients with bilateral disease, the side of implantation is most likely to occur in the worst hearing ear (Lustig et al., 2003)., although this may be unclear in some cases. Some evidence supports bilateral CI of MD patients as this may achieve better speech outcomes, as is the case in non-MD populations (Holden et al., 2012; Lustig et al., 2003). It is however unclear what effect this may have on a patient's ability to compensate for vestibular damage. In the future if UK NICE guidance extends its criteria to offering bilateral implantation for profound bilateral deafness in adults, it may be pertinent to perform vestibular function tests to help minimise post op complications such as bilateral vestibular hypofunction.

At our institution, choice of MH arrays are generally reserved for patients with far advanced otosclerosis to minimise non-auditory stimulation due to low current utilisation, or for inner ear malformations in order to minimise the risk of electrode migration by conforming to the modiolus. It is well documented that current levels may vary according to aetiology of hearing loss, such as a higher threshold requirement for inner ear malformations, meningitis, cochlear nerve hypoplasia or enlarged vestibular aqueduct. These differences may be explained by electrode position relative to neural elements or neural degeneration (Incerti et al., 2018). For this reason, it may be theoretically favourable for MH arrays to be used in MD patients to facilitate re-mapping with a larger dynamic range. In our study, only 4 patients underwent implantation with MH arrays (surgeon's preference) which had no impact on post-operative speech outcomes or a preponderance to being in the post-operative MD+ group; however the numbers are too small to draw conclusions.

Optimal insertion depth is determined by balancing factors such as cochlear coverage, insertional trauma and residual hearing. Cochlear coverage can range between 360 and 450 degrees for both LW and MH arrays (Risi 2018; Dhanasingh et al., 2017), and given that impedances changes in MD may target more distal electrodes (as in the case report above), the use of shorter or medium length electrodes may be more appropriate in the MD group, although this needs to be balanced against the theoretical advantages of deep insertion. With increasing utilisation of cone beam computer tomography following implantation, we may be able to more accurately determine the optimum insertion depth according to individual cochlea duct length which may influence overall outcome.

*Limitations of study*

Cochlear implant performance is dependent on a number of factors such as: duration of deafness, age at implantation, patient motivation and primary mode of communication. Although groups were matched for age, biological sex and device type, there are likely to have been discrepancies amongst the MD and control groups that may have influenced auditory performance. We also appreciate that following switch-on, most mapping requirements will generally increase for up to a period of 6 weeks, however, attempts were made to correct for this in each group through the calculation of expected visits based on the hospital protocol. In addition, there may have also been inherently differing rates of dizziness/vertigo within the control group necessitating an increase in audiology visits. Although the results demonstrate better overall speech scores within the MD group, this may have been secondary to better pre-operative hearing thresholds or better levels of residual hearing post implantation. Ideally, follow up between groups should have also been matched (in addition to age, biological sex and electrode design), but due to relatively low numbers, this was not possible.

*Future considerations*

Further work on mapping strategies and impedance patterns is currently being undertaken at our institution on patients with MD. Other future considerations will focus on exploring the ideal electrode insertion depth to examine whether shorter or medium length arrays minimise electrical disruption in the more distal electrodes, and comparative outcomes between MH and LW electrodes.

## Conclusion

Cochlear implantation is a safe procedure in patients with MD. Our results demonstrate that although CI in patients with MD does not trigger an activation of quiescent MD (irrespective of whether unilaterally or bilaterally performed), those with active MD pre-operatively may be at risk of requiring prolonged periods of auditory rehabilitation which may impact their quality of life. Patients with MD may achieve higher speech scores following CI when compared with non-MD patients. We emphasise the importance of pre-operative counselling to be offered to all patients with MD in order to better address expectations following surgery with reference to the likelihood of ongoing auditory rehabilitation following surgery. Evidence suggests that ablative treatment prior to cochlear implantation improves outcomes without adversely affecting speech scores. It remains unclear whether the insertion of pre-curved electrodes may facilitate re-mapping due to the utilisation of lower currents compared to lateral wall arrays.

## Declaration of interest

None

## Word count

2984

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**ABSTRACT**

*Objective:* To perform a matched cohort study to assess whether patients with Meniere's Disease (MD) require more intensive auditory rehabilitation following cochlear implantation and identify factors(s) that may affect outcomes in patients with MD.

*Methods:* A retrospective case review was performed using electronic/paper records and departmental database. All MD and control patients were matched for age, biological sex, implant manufacturer and electrode design. Variables measured include: age at implantation, duration of deafness pre-implantation, pre- and post-operative MD state (whether 'active' MD+ or 'inactive' MD-), laterality of implantation relative to disease side, pre- and post-operative ablative treatment, and electrode design. Outcomes measured were speech scores, number of visits to audiology department following switch-on, and post-operative progression to active MD.

*Results:* Forty consecutive implanted MD patients were identified between May 1993 and May 2019. Although post-operative speech scores in MD patients were comparable to those within the control group, patients with active MD following implantation required significantly more visits to the audiology department compared to both controls ($p<0.01$) and patients who had inactive MD post-operatively ($p<0.01$). However, in MD patients, active MD was less likely following CI surgery ($p=0.03$). This is because fifty-five percent of patients with pre-operative active Meniere's disease ceased to experience active Meniere's disease post-operatively, while none of the patients with inactive MD prior to implantation progressed to active Meniere's disease post-operatively. In those patients who continued to

experience active MD post-operatively, further medical and surgical ablative intervention was required to control ongoing Meniere's attacks.

*Conclusion:* We present the largest case series of performance outcomes in CI patients with MD. Although speech outcomes in MD patients are comparable to controls, patients with active MD pre-operatively are more likely to experience variation in CI performance requiring a prolonged period of auditory rehabilitation compared to inactive pre-operative MD.

*Keywords:* Meniere's disease, cochlear implantation, impedances, hospital visits, speech scores

## INTRODUCTION

Profound bilateral hearing loss may occur in patients with Meniere's Disease (MD) due to end stage disease or loss of hearing following ablation of the inner ear. Many studies have demonstrated that patients with MD undergoing cochlear implantation (CI) may develop comparable or above average auditory performance scores compared with non-MD patients. (Manrique-Huarte et al., 2018, Lustig et al., 2003; Mick et al., 2014 ) as well as improved tinnitus scores (Mick et al., 2014; Vermeire et al., 2014; Richardson et al., 2014). Following discussions with audiology colleagues both locally, and at national level within the British Cochlear Implant Group, it is widely recognised that this particular cohort of patients do present challenges with respect to post-operative programming due to ongoing distortions in auditory perception. Evidence based on small case series confirms high levels of auditory fluctuations which manifest as variations in cochlear implant performance (Holden et al., 2012; McNeill et al., 2016; Samy et al., 2016). High levels of impedance have also been noted in patients with active MD which has necessitated adjustments in implant mapping on a long term basis following initial rehabilitation (Holden et al., 2012; McNeill et al., 2016; Samy et al., 2016). This, in turn, may adversely impact quality of life and place greater demand on audiology-led services.

To confirm whether patients with Meniere's Disease (MD) require more intensive auditory rehabilitation and identify factors(s) that may contribute to variable cochlear implant performance in patients with MD. we performed a large retrospective review of all MD patients who underwent CI at our Institution.

## Methods

A retrospective review of all patients with MD undergoing cochlear implantation at a tertiary referral centre in London was conducted. Information was retrieved from Bawtry Computer Systems (BCS) database, electronic health records (EPIC Systems Corporation) and paper records. A control group of non-MD patients undergoing CI was included to evaluate any difference in outcomes between the two groups. In order to minimise any confounding effect, all patients in the control group were matched for age, biological sex (with one exception), implant manufacturer, electrode design and age at implantation with those in the MD group (ratio 1:1). Electrode arrays were classified as "straight/lateral wall" (LW) or "pre-curved/modiolar hugging"(MH). All cochlear implant surgery was performed using an atraumatic approach to maximise audiometric and vestibular outcomes post operatively.

### *Inclusion criteria*

All patients with a diagnosis of MD consistent with the AAO-HNS 1995, 2015 or 2020 definition were included in the series (Basura et al., 2020). The latest version of this criteria summarises patients into 2 categories; 'Definite MD and Probable MD'. Patients were classified into the 'active' post-operative group (MD+) if they exhibited subjective auditory fluctuations (i.e. changes in cochlear implant performance) in the presence or absence of vertigo and tinnitus. All patients satisfied audiometric and speech thresholds in line with national guidance (National Institute of Clinical Excellence, NICE) prior to 2019 to be deemed suitable for CI.

*Data fields*

Variables assessed included: duration of deafness pre-implantation; pre and post-operative MD state (active MD+/inactive MD-); laterality of implantation relative to affected MD side; relevant past medical history (visual impairment, vestibular migraine, superior semi-circular canal dehiscence, severe musculoskeletal disease), causes of hearing loss (e.g. meningitis, rubella, measles etc.); balance testing; pre and post-operative ablative treatment; electrode design; post-operative complications; pre and post-operative speech scores; and number of visits to the audiology from the switch-on to latest follow up.

Speech scores were measured using Bamford-Kowal-Bench testing (BKBs) in quiet. The number of expected visits to audiology following implantation was calculated using the standard hospital protocol of 4-5 appointments within 3 months following implantation, then a yearly and 2 yearly review. The number of visits was presented as a percentage of 'normalised visits' using the following equation: 100 x (number of visits – number of expected visits)/number of expected visits. This means that when percentage of hospital visits is '0', it is aligned with the expected number of visits according to the hospital protocol. The number of visits was corrected for between the MD and control group based on time of implantation or transfer-in to hospital and the duration of follow-up

*Statistical analysis*

Statistical analysis was performed using two-tailed Chi-square tests, Mann Whitney U tests or Wilcoxon signed-rank tests, with Bonferroni correction used to correct for multiple comparisons.

## Results

Forty patients (18 females, 22 males) met the study inclusion criteria and were implanted between May 1993 and May 2019. The mean age at implantation was 62 years old (range: 26- 94 years) and mean follow up was 6.5 years (range: 6 months- 26 years). Table 1 compares the characteristics and demographics for MD and control groups.

*Disease activity following cochlear implantation*

To assess the impact of cochlear implantation on MD symptoms, we investigated the prevalence of active MD post-operatively with that observed pre-operatively (Figure 1). In the pre-operative period, twenty-nine patients (72.5%) were MD+ compared with 7 (17.5%) MD- patients. Data on disease activity was unavailable for 4 patients (10%). Overall, we found that the prevalence of active MD was significantly reduced following CI surgery ($p=0.03$, chi-squared test). This is because 55% of the patients with active MD before implantation ceased to experience active MD post-operatively. In addition, none of the patients with inactive MD prior to implantation progressed to active MD post-operatively. A precise breakdown of these results (and the number of patients corresponding to each group) is illustrated in Figure 1. In patients who continued to experience active MD following CI (13/29; 45%), a minority (4/13; 31%) also required further treatment (including ablation) for active disease.

*Number of post-operative visits to audiology depends on MD status*

To assess the audiological needs of MD patients following cochlear implantation, we next examined the number of post-operative visits to audiology for both MD+ and MD- patients. More specifically, we asked whether the number of visits to audiology was greater than that

expected for controls (Figure 2; see methods for details of how numbers of visits were normalized relative to expectations). We found that post-operative MD+ patients visited audiology departments more often than both post-operative MD- patients ($p<0.01$; Mann-Whitney U test) and controls ($p<0.01$; Wilcoxon signed-rank test). However, whilst post-operative MD- patients tended to visit audiology departments slightly more often than controls, this trend was not significant ($p>0.05$; Wilcoxon signed-rank test). In addition, no significant difference was found between MD patients with unilateral or bilateral MD (see Table 2 for a list of additional characteristics in MD patients that did not affect outcomes).

*Speech comprehension outcomes do not depend on post-operative MD status*

Since post-operative MD+ patients visit audiological services more often than controls, we next considered whether this might be because their speech comprehension outcomes are worse than either controls or MD- patients. However, whilst there was a slight trend for MD patients (particularly MD- patients) to do slightly better overall (Figure 3a), post-operative speech scores did not depend on MD status, with no significant difference between MD+ and MD- patients ($p>0.05$, Mann-Whitney U test). There were also no significant differences between either the MD+ group and controls or the MD- group and controls ($p>0.05$; Wilcoxon signed-rank tests). Consistent with this, the improvement in speech scores following implantation was also similar for different patient groups (Figure 3b; no significant differences between groups; $p>0.05$), albeit slightly higher for the MD patients (particularly MD- patients). Consequently, when we compared the improvement in speech scores across groups, there was no significant difference between the MD+ and MD- groups (Mann-Whitney U test; $p>0.05$), and there were no significant differences between either the MD+ group and controls or the MD- group and controls (Wilcoxon signed-rank tests; $p>0.05$).

*Disease laterality and side of implantation*

Thirty-seven patients underwent unilateral cochlear implantation and 3 underwent bilateral cochlear implantation. Reasons for bilateral implantation included visual impairment and soft failure on initial side. Five patients underwent cochlear implantation in the ear contralateral to the MD ear. The rationale for contralateral implantation was variable, including: disease burn out in the ipsilateral side, soft failure on the ipsilateral side necessitating sequential surgery on the active side, dead ear on the ipsilateral side and declining hearing in the contralateral ear. Three out of the 5 patients went on to have active disease. A more comprehensive breakdown of these findings is shown in Table 3. There was no significant difference in the number of post-operative visits between the ipsilaterally implanted group (n=35) and the contralaterally implanted group (n=5) (median visits 37.5 and 55.6 respectively, p=0.90, Mann Whitney test, see Table 2).

*Other Domains and complications*

Other variables assessed in the study made no significant difference to outcome and are outlined in Table 2.

**Discussion**

The aim of this study was to better understand how various factors shape CI outcomes in MD patients, using the largest case series of this type published to date. Following implantation, we measured the number of visits to audiology, speech comprehension outcomes, and the prevalence of active MD.

Our data clearly demonstrate that patients with post-operative MD+ required significantly more visits to the audiology department compared to controls. In the majority of instances,

the purpose of these visits was to troubleshoot distortions in auditory perception experienced by the patient which were thought to be related to ongoing active episodes of MD . In many cases this would require reprogramming of the device to improve the sound quality. Patients in the postoperative MD- group had slightly more visits than the controls, but these differences were not significant. It is therefore advisable that all MD patients are counselled that they are likely to require a prolonged period of rehabilitation following implantation. Although our results do not identify the reasons for this, previous studies suggest that patients with on-going fluctuations in hearing demonstrate increased impedances and ongoing mapping requirements (Samy et al., 2016). What is not clear is why these fluctuations arise. A possible explanation may be that the presence of intracochlear fibrosis following implantation may render the endolymphatic space more susceptible to hydrops (Fife et al., 2014; Lustig et al., 2003). Another possibility could be due to on-going vestibular dysfunction caused by autoimmune MD due to changes in vestibular physiology following implantation (Lesinski et al., 1998). Several reports in the literature describe increases in impedances during so called 'Meniere's attacks' (Holden et al., 2012; McNeill et al., 2016; Samy et al., 2016). One such study reports significantly larger impedances (>3 kohms) in the symptomatic MD side of a patient with bilateral cochlear implants (Samy et al., 2016). Over a 9-year follow up of this patient, only one episode of vertigo was experienced compared with multiple attacks of tinnitus during impedance increases, suggesting that changes in electrical stimulation are perceived by the auditory cortex (McNeill et al., 2016). The increases in impedance were found to consistently affect the more distal electrodes (9-16) which corresponded to the mid frequency range. The authors discovered that current recalibration within this range overcame the changes in impedance. The specific mapping strategies used to achieve this are unclear, and indeed our institutional experience has found that anecdotally some patients required an increased dynamic range, while others a reduction.

In our study, patients with MD tended to achieve higher post-operative speech scores when compared to controls. Even though this result seems to corroborate previous findings (Mick et al. 2014; Vermiere et al., 2014), this difference was found to be not statistically significant ($p=0.12$) in our analysis. Despite only 2 patients undergoing surgical ablation pre-operatively, this did not impact on post-operative speech scores when compared with matched controls, supporting the idea that ablative treatment prior to CI could be considered a reasonable option in this category of patients (Holden et al. 2012). In this regard, some authors suggest simultaneous labyrinthectomy with the aim to remove the environment where on-going disease can ensue (Foster et al., 2013; Lustig et al., 2003; Hansen et al., 2013; Doobe et al., 2015). In our case series, only one patient underwent endolymphatic decompression following CI and, therefore, conclusions on cochlear implant outcomes in this particular case could not be drawn. However, as a general rule, we advise to avoid any surgical treatment following CI as this may affect/alter the implant.

In this study, the prevalence of active MD was reduced following cochlear implantation. This was partly because no patients with inactive Meniere's disease preoperatively developed active Meniere's disease postoperatively suggesting CI surgery does not trigger activation of quiescent Meniere's disease. It would therefore appear that patients with pre-operative active disease are therefore most at risk of experiencing ongoing symptoms, however, it is possible that biochemical changes with the cochlear following implantation may potentially stimulate symptoms of MD in the pre-operative MD- group. The reduction in active MD prevalence following implantation was primarily because just over half (55%) of patients with active Meniere's disease preoperatively did not have active disease after cochlear implantation.

Nevertheless, forty-five percent of patients with pre-operative active Meniere's disease continued to have disease activity in the post-operative phase, with 4 of these patients requiring further treatment (including ablation) for active disease following implantation. All surgery was performed using an atraumatic approach in order to preserve audiometric and vestibular function.

We did not observe any significant differences between bilateral and unilateral CI in MD patients developing post-operative MD+ as additionally proven by our 10 patients who had confirmed pre-operative bilateral hypofunction. Although 3 out of 5 patients continued to have MD+ following implantation (Table 2), this difference was also not significant and had no impact on the number of post-operative visits to audiology.

By convention, the side of implantation will occur on the ipsilateral side of disease in order to preserve vestibular function in the contralateral ear which is assumed to have better vestibular function, Hence this should reduce the impact on balance in the post-operative period. For patients with bilateral disease, the side of implantation is most likely to occur in the worst hearing ear (Lustig et al., 2003)., although this may be unclear in some cases. Some evidence supports bilateral CI of MD patients as this may achieve better speech outcomes, as is the case in non-MD populations (Holden et al., 2012; Lustig et al., 2003). It is however unclear what effect this may have on a patient's ability to compensate for vestibular damage. In the future if UK NICE guidance extends its criteria to offering bilateral implantation for profound bilateral deafness in adults, it may be pertinent to perform vestibular function tests to help minimise post op complications such as bilateral vestibular hypofunction.

At our institution, choice of MH arrays are generally reserved for patients with far advanced otosclerosis to minimise non-auditory stimulation due to low current utilisation, or for inner ear malformations in order to minimise the risk of electrode migration by conforming to the modiolus. It is well documented that current levels may vary according to aetiology of hearing loss, such as a higher threshold requirement for inner ear malformations, meningitis, cochlear nerve hypoplasia or enlarged vestibular aqueduct. These differences may be explained by electrode position relative to neural elements or neural degeneration (Incerti et al., 2018). For this reason, it may be theoretically favourable for MH arrays to be used in MD patients to facilitate re-mapping with a larger dynamic range. In our study, only 4 patients underwent implantation with MH arrays (surgeon's preference) which had no impact on post-operative speech outcomes or a preponderance to being in the post-operative MD+ group; however the numbers are too small to draw conclusions.

Optimal insertion depth is determined by balancing factors such as cochlear coverage, insertional trauma and residual hearing. Cochlear coverage can range between 360 and 450 degrees for both LW and MH arrays (Risi 2018; Dhanasingh et al., 2017), and given that impedances changes in MD may target more distal electrodes (as in the case report above), the use of shorter or medium length electrodes may be more appropriate in the MD group, although this needs to be balanced against the theoretical advantages of deep insertion. With increasing utilisation of cone beam computer tomography following implantation, we may be able to more accurately determine the optimum insertion depth according to individual cochlea duct length which may influence overall outcome.

*Limitations of study*

Cochlear implant performance is dependent on a number of factors such as: duration of deafness, age at implantation, patient motivation and primary mode of communication. Although groups were matched for age, biological sex and device type, there are likely to have been discrepancies amongst the MD and control groups that may have influenced auditory performance. We also appreciate that following switch-on, most mapping requirements will generally increase for up to a period of 6 weeks, however, attempts were made to correct for this in each group through the calculation of expected visits based on the hospital protocol. In addition, there may have also been inherently differing rates of dizziness/vertigo within the control group necessitating an increase in audiology visits. Although the results demonstrate better overall speech scores within the MD group, this may have been secondary to better pre-operative hearing thresholds or better levels of residual hearing post implantation. Ideally, follow up between groups should have also been matched (in addition to age, biological sex and electrode design), but due to relatively low numbers, this was not possible.

*Future considerations*

Further work on mapping strategies and impedance patterns is currently being undertaken at our institution on patients with MD. Other future considerations will focus on exploring the ideal electrode insertion depth to examine whether shorter or medium length arrays minimise electrical disruption in the more distal electrodes, and comparative outcomes between MH and LW electrodes.

## Conclusion

Cochlear implantation is a safe procedure in patients with MD. Our results demonstrate that although CI in patients with MD does not trigger an activation of quiescent MD (irrespective of whether unilaterally or bilaterally performed), those with active MD pre-operatively may be at risk of requiring prolonged periods of auditory rehabilitation which may impact their quality of life. Patients with MD may achieve higher speech scores following CI when compared with non-MD patients. We emphasise the importance of pre-operative counselling to be offered to all patients with MD in order to better address expectations following surgery with reference to the likelihood of ongoing auditory rehabilitation following surgery. Evidence suggests that ablative treatment prior to cochlear implantation improves outcomes without adversely affecting speech scores. It remains unclear whether the insertion of pre-curved electrodes may facilitate re-mapping due to the utilisation of lower currents compared to lateral wall arrays.

## Declaration of interest

None

## Word count

2984

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Response to comments:

Thank you for your comments. I addressed the minor issues outlined below.

Kind regards,

1. Please specify if you mean biological sex or gender in the participant section.

- I have amended this to biological sex

2. Please include outcomes of the comparison of MD+ and the control group for the speech recognition outcomes.

Under the section '*Speech comprehension outcomes do not depend on post-operative MD status'* I have clarified this area further.

- There were also no significant differences between either the MD+ group and controls or the MD- group and controls ($p>0.05$; Wilcoxon signed-rank tests). Consistent with this, the improvement in speech scores following implantation was also similar for different patient groups (Figure 3b; no significant differences between groups; $p>0.05$), albeit slightly higher for the MD patients (particularly MD- patients). Consequently, when we compared the improvement in speech scores across groups, there was no significant difference between the MD+ and MD- groups (Mann-Whitney U test; $p>0.05$), and there were no significant differences between either the MD+ group and controls or the MD- group and controls (Wilcoxon signed-rank tests; $p>0.05$).
-

**ABSTRACT**

*Objective:* To perform a matched cohort study to assess whether patients with Meniere's Disease (MD) require more intensive auditory rehabilitation following cochlear implantation and identify factors(s) that may affect outcomes in patients with MD.

*Methods:* A retrospective case review was performed using electronic/paper records and departmental database. All MD and control patients were matched for age, biological sex, implant manufacturer and electrode design. Variables measured include: age at implantation, duration of deafness pre-implantation, pre- and post-operative MD state (whether 'active' MD+ or 'inactive' MD-), laterality of implantation relative to disease side, pre- and post-operative ablative treatment, and electrode design. Outcomes measured were speech scores, number of visits to audiology department following switch-on, and post-operative progression to active MD.

*Results:* Forty consecutive implanted MD patients were identified between May 1993 and May 2019. Although post-operative speech scores in MD patients were comparable to those within the control group, patients with active MD following implantation required significantly more visits to the audiology department compared to both controls ($p<0.01$) and patients who had inactive MD post-operatively ($p<0.01$). However, in MD patients, active MD was less likely following CI surgery ($p=0.03$). This is because fifty-five percent of patients with pre-operative active Meniere's disease ceased to experience active Meniere's disease post-operatively, while none of the patients with inactive MD prior to implantation progressed to active Meniere's disease post-operatively. In those patients who continued to

experience active MD post-operatively, further medical and surgical ablative intervention was required to control ongoing Meniere's attacks.

*Conclusion:* We present the largest case series of performance outcomes in CI patients with MD. Although speech outcomes in MD patients are comparable to controls, patients with active MD pre-operatively are more likely to experience variation in CI performance requiring a prolonged period of auditory rehabilitation compared to inactive pre-operative MD.

*Keywords:* Meniere's disease, cochlear implantation, impedances, hospital visits, speech scores

## INTRODUCTION

Profound bilateral hearing loss may occur in patients with Meniere's Disease (MD) due to end stage disease or loss of hearing following ablation of the inner ear. Many studies have demonstrated that patients with MD undergoing cochlear implantation (CI) may develop comparable or above average auditory performance scores compared with non-MD patients. (Manrique-Huarte et al., 2018, Lustig et al., 2003; Mick et al., 2014 ) as well as improved tinnitus scores (Mick et al., 2014; Vermeire et al., 2014; Richardson et al., 2014). Following discussions with audiology colleagues both locally, and at national level within the British Cochlear Implant Group, it is widely recognised that this particular cohort of patients do present challenges with respect to post-operative programming due to ongoing distortions in auditory perception. Evidence based on small case series confirms high levels of auditory fluctuations which manifest as variations in cochlear implant performance (Holden et al., 2012; McNeill et al., 2016; Samy et al., 2016). High levels of impedance have also been noted in patients with active MD which has necessitated adjustments in implant mapping on a long term basis following initial rehabilitation (Holden et al., 2012; McNeill et al., 2016; Samy et al., 2016). This, in turn, may adversely impact quality of life and place greater demand on audiology-led services.

To confirm whether patients with Meniere's Disease (MD) require more intensive auditory rehabilitation and identify factors(s) that may contribute to variable cochlear implant performance in patients with MD. we performed a large retrospective review of all MD patients who underwent CI at our Institution.

## Methods

A retrospective review of all patients with MD undergoing cochlear implantation at a tertiary referral centre in London was conducted. Information was retrieved from Bawtry Computer Systems (BCS) database, electronic health records (EPIC Systems Corporation) and paper records. A control group of non-MD patients undergoing CI was included to evaluate any difference in outcomes between the two groups. In order to minimise any confounding effect, all patients in the control group were matched for age, biological sex (with one exception), implant manufacturer, electrode design and age at implantation with those in the MD group (ratio 1:1). Electrode arrays were classified as "straight/lateral wall" (LW) or "pre-curved/modiolar hugging"(MH). All cochlear implant surgery was performed using an atraumatic approach to maximise audiometric and vestibular outcomes post operatively.

### *Inclusion criteria*

All patients with a diagnosis of MD consistent with the AAO-HNS 1995, 2015 or 2020 definition were included in the series (Basura et al., 2020). The latest version of this criteria summarises patients into 2 categories; 'Definite MD and Probable MD'. Patients were classified into the 'active' post-operative group (MD+) if they exhibited subjective auditory fluctuations (i.e. changes in cochlear implant performance) in the presence or absence of vertigo and tinnitus. All patients satisfied audiometric and speech thresholds in line with national guidance (National Institute of Clinical Excellence, NICE) prior to 2019 to be deemed suitable for CI.

*Data fields*

Variables assessed included: duration of deafness pre-implantation; pre and post-operative MD state (active MD+/inactive MD-); laterality of implantation relative to affected MD side; relevant past medical history (visual impairment, vestibular migraine, superior semi-circular canal dehiscence, severe musculoskeletal disease), causes of hearing loss (e.g. meningitis, rubella, measles etc.); balance testing; pre and post-operative ablative treatment; electrode design; post-operative complications; pre and post-operative speech scores; and number of visits to the audiology from the switch-on to latest follow up.

Speech scores were measured using Bamford-Kowal-Bench testing (BKBs) in quiet. The number of expected visits to audiology following implantation was calculated using the standard hospital protocol of 4-5 appointments within 3 months following implantation, then a yearly and 2 yearly review. The number of visits was presented as a percentage of 'normalised visits' using the following equation: 100 x (number of visits – number of expected visits)/number of expected visits. This means that when percentage of hospital visits is '0', it is aligned with the expected number of visits according to the hospital protocol. The number of visits was corrected for between the MD and control group based on time of implantation or transfer-in to hospital and the duration of follow-up

*Statistical analysis*

Statistical analysis was performed using two-tailed Chi-square tests, Mann Whitney U tests or Wilcoxon signed-rank tests, with Bonferroni correction used to correct for multiple comparisons.

## Results

Forty patients (18 females, 22 males) met the study inclusion criteria and were implanted between May 1993 and May 2019. The mean age at implantation was 62 years old (range: 26- 94 years) and mean follow up was 6.5 years (range: 6 months- 26 years). Table 1 compares the characteristics and demographics for MD and control groups.

*Disease activity following cochlear implantation*

To assess the impact of cochlear implantation on MD symptoms, we investigated the prevalence of active MD post-operatively with that observed pre-operatively (Figure 1). In the pre-operative period, twenty-nine patients (72.5%) were MD+ compared with 7 (17.5%) MD- patients. Data on disease activity was unavailable for 4 patients (10%). Overall, we found that the prevalence of active MD was significantly reduced following CI surgery ($p=0.03$, chi-squared test). This is because 55% of the patients with active MD before implantation ceased to experience active MD post-operatively. In addition, none of the patients with inactive MD prior to implantation progressed to active MD post-operatively. A precise breakdown of these results (and the number of patients corresponding to each group) is illustrated in Figure 1. In patients who continued to experience active MD following CI (13/29; 45%), a minority (4/13; 31%) also required further treatment (including ablation) for active disease.

*Number of post-operative visits to audiology depends on MD status*

To assess the audiological needs of MD patients following cochlear implantation, we next examined the number of post-operative visits to audiology for both MD+ and MD- patients. More specifically, we asked whether the number of visits to audiology was greater than that

expected for controls (Figure 2; see methods for details of how numbers of visits were normalized relative to expectations). We found that post-operative MD+ patients visited audiology departments more often than both post-operative MD- patients ($p<0.01$; Mann-Whitney U test) and controls ($p<0.01$; Wilcoxon signed-rank test). However, whilst post-operative MD- patients tended to visit audiology departments slightly more often than controls, this trend was not significant ($p>0.05$; Wilcoxon signed-rank test). In addition, no significant difference was found between MD patients with unilateral or bilateral MD (see Table 2 for a list of additional characteristics in MD patients that did not affect outcomes).

*Speech comprehension outcomes do not depend on post-operative MD status*

Since post-operative MD+ patients visit audiological services more often than controls, we next considered whether this might be because their speech comprehension outcomes are worse than either controls or MD- patients. However, whilst there was a slight trend for MD patients (particularly MD- patients) to do slightly better overall (Figure 3a), post-operative speech scores did not depend on MD status, with no significant difference between MD+ and MD- patients ($p>0.05$, Mann-Whitney U test). There were also no significant differences between either the MD+ group and controls or the MD- group and controls ($p>0.05$; Wilcoxon signed-rank tests). Consistent with this, the improvement in speech scores following implantation was also similar for different patient groups (Figure 3b; no significant differences between groups; $p>0.05$), albeit slightly higher for the MD patients (particularly MD- patients). Consequently, when we compared the improvement in speech scores across groups, there was no significant difference between the MD+ and MD- groups (Mann-Whitney U test; $p>0.05$), and there were no significant differences between either the MD+ group and controls or the MD- group and controls (Wilcoxon signed-rank tests; $p>0.05$).

*Disease laterality and side of implantation*

Thirty-seven patients underwent unilateral cochlear implantation and 3 underwent bilateral cochlear implantation. Reasons for bilateral implantation included visual impairment and soft failure on initial side. Five patients underwent cochlear implantation in the ear contralateral to the MD ear. The rationale for contralateral implantation was variable, including: disease burn out in the ipsilateral side, soft failure on the ipsilateral side necessitating sequential surgery on the active side, dead ear on the ipsilateral side and declining hearing in the contralateral ear. Three out of the 5 patients went on to have active disease. A more comprehensive breakdown of these findings is shown in Table 3. There was no significant difference in the number of post-operative visits between the ipsilaterally implanted group (n=35) and the contralaterally implanted group (n=5) (median visits 37.5 and 55.6 respectively, p=0.90, Mann Whitney test, see Table 2).

*Other Domains and complications*

Other variables assessed in the study made no significant difference to outcome and are outlined in Table 2.

**Discussion**

The aim of this study was to better understand how various factors shape CI outcomes in MD patients, using the largest case series of this type published to date. Following implantation, we measured the number of visits to audiology, speech comprehension outcomes, and the prevalence of active MD.

Our data clearly demonstrate that patients with post-operative MD+ required significantly more visits to the audiology department compared to controls. In the majority of instances,

the purpose of these visits was to troubleshoot distortions in auditory perception experienced by the patient which were thought to be related to ongoing active episodes of MD . In many cases this would require reprogramming of the device to improve the sound quality. Patients in the postoperative MD- group had slightly more visits than the controls, but these differences were not significant. It is therefore advisable that all MD patients are counselled that they are likely to require a prolonged period of rehabilitation following implantation. Although our results do not identify the reasons for this, previous studies suggest that patients with on-going fluctuations in hearing demonstrate increased impedances and ongoing mapping requirements (Samy et al., 2016). What is not clear is why these fluctuations arise. A possible explanation may be that the presence of intracochlear fibrosis following implantation may render the endolymphatic space more susceptible to hydrops (Fife et al., 2014; Lustig et al., 2003). Another possibility could be due to on-going vestibular dysfunction caused by autoimmune MD due to changes in vestibular physiology following implantation (Lesinski et al., 1998). Several reports in the literature describe increases in impedances during so called 'Meniere's attacks' (Holden et al., 2012; McNeill et al., 2016; Samy et al., 2016). One such study reports significantly larger impedances (>3 kohms) in the symptomatic MD side of a patient with bilateral cochlear implants (Samy et al., 2016). Over a 9-year follow up of this patient, only one episode of vertigo was experienced compared with multiple attacks of tinnitus during impedance increases, suggesting that changes in electrical stimulation are perceived by the auditory cortex (McNeill et al., 2016). The increases in impedance were found to consistently affect the more distal electrodes (9-16) which corresponded to the mid frequency range. The authors discovered that current recalibration within this range overcame the changes in impedance. The specific mapping strategies used to achieve this are unclear, and indeed our institutional experience has found that anecdotally some patients required an increased dynamic range, while others a reduction.

In our study, patients with MD tended to achieve higher post-operative speech scores when compared to controls. Even though this result seems to corroborate previous findings (Mick et al. 2014; Vermiere et al., 2014), this difference was found to be not statistically significant ($p=0.12$) in our analysis. Despite only 2 patients undergoing surgical ablation pre-operatively, this did not impact on post-operative speech scores when compared with matched controls, supporting the idea that ablative treatment prior to CI could be considered a reasonable option in this category of patients (Holden et al. 2012). In this regard, some authors suggest simultaneous labyrinthectomy with the aim to remove the environment where on-going disease can ensue (Foster et al., 2013; Lustig et al., 2003; Hansen et al., 2013; Doobe et al., 2015). In our case series, only one patient underwent endolymphatic decompression following CI and, therefore, conclusions on cochlear implant outcomes in this particular case could not be drawn. However, as a general rule, we advise to avoid any surgical treatment following CI as this may affect/alter the implant.

In this study, the prevalence of active MD was reduced following cochlear implantation. This was partly because no patients with inactive Meniere's disease preoperatively developed active Meniere's disease postoperatively suggesting CI surgery does not trigger activation of quiescent Meniere's disease. It would therefore appear that patients with pre-operative active disease are therefore most at risk of experiencing ongoing symptoms, however, it is possible that biochemical changes with the cochlear following implantation may potentially stimulate symptoms of MD in the pre-operative MD- group. The reduction in active MD prevalence following implantation was primarily because just over half (55%) of patients with active Meniere's disease preoperatively did not have active disease after cochlear implantation.

Nevertheless, forty-five percent of patients with pre-operative active Meniere's disease continued to have disease activity in the post-operative phase, with 4 of these patients requiring further treatment (including ablation) for active disease following implantation. All surgery was performed using an atraumatic approach in order to preserve audiometric and vestibular function.

We did not observe any significant differences between bilateral and unilateral CI in MD patients developing post-operative MD+ as additionally proven by our 10 patients who had confirmed pre-operative bilateral hypofunction. Although 3 out of 5 patients continued to have MD+ following implantation (Table 2), this difference was also not significant and had no impact on the number of post-operative visits to audiology.

By convention, the side of implantation will occur on the ipsilateral side of disease in order to preserve vestibular function in the contralateral ear which is assumed to have better vestibular function, Hence this should reduce the impact on balance in the post-operative period. For patients with bilateral disease, the side of implantation is most likely to occur in the worst hearing ear (Lustig et al., 2003)., although this may be unclear in some cases. Some evidence supports bilateral CI of MD patients as this may achieve better speech outcomes, as is the case in non-MD populations (Holden et al., 2012; Lustig et al., 2003). It is however unclear what effect this may have on a patient's ability to compensate for vestibular damage. In the future if UK NICE guidance extends its criteria to offering bilateral implantation for profound bilateral deafness in adults, it may be pertinent to perform vestibular function tests to help minimise post op complications such as bilateral vestibular hypofunction.

At our institution, choice of MH arrays are generally reserved for patients with far advanced otosclerosis to minimise non-auditory stimulation due to low current utilisation, or for inner ear malformations in order to minimise the risk of electrode migration by conforming to the modiolus. It is well documented that current levels may vary according to aetiology of hearing loss, such as a higher threshold requirement for inner ear malformations, meningitis, cochlear nerve hypoplasia or enlarged vestibular aqueduct. These differences may be explained by electrode position relative to neural elements or neural degeneration (Incerti et al., 2018). For this reason, it may be theoretically favourable for MH arrays to be used in MD patients to facilitate re-mapping with a larger dynamic range. In our study, only 4 patients underwent implantation with MH arrays (surgeon's preference) which had no impact on post-operative speech outcomes or a preponderance to being in the post-operative MD+ group; however the numbers are too small to draw conclusions.

Optimal insertion depth is determined by balancing factors such as cochlear coverage, insertional trauma and residual hearing. Cochlear coverage can range between 360 and 450 degrees for both LW and MH arrays (Risi 2018; Dhanasingh et al., 2017), and given that impedances changes in MD may target more distal electrodes (as in the case report above), the use of shorter or medium length electrodes may be more appropriate in the MD group, although this needs to be balanced against the theoretical advantages of deep insertion. With increasing utilisation of cone beam computer tomography following implantation, we may be able to more accurately determine the optimum insertion depth according to individual cochlea duct length which may influence overall outcome.

*Limitations of study*

Cochlear implant performance is dependent on a number of factors such as: duration of deafness, age at implantation, patient motivation and primary mode of communication. Although groups were matched for age, biological sex and device type, there are likely to have been discrepancies amongst the MD and control groups that may have influenced auditory performance. We also appreciate that following switch-on, most mapping requirements will generally increase for up to a period of 6 weeks, however, attempts were made to correct for this in each group through the calculation of expected visits based on the hospital protocol. In addition, there may have also been inherently differing rates of dizziness/vertigo within the control group necessitating an increase in audiology visits. Although the results demonstrate better overall speech scores within the MD group, this may have been secondary to better pre-operative hearing thresholds or better levels of residual hearing post implantation. Ideally, follow up between groups should have also been matched (in addition to age, biological sex and electrode design), but due to relatively low numbers, this was not possible.

*Future considerations*

Further work on mapping strategies and impedance patterns is currently being undertaken at our institution on patients with MD. Other future considerations will focus on exploring the ideal electrode insertion depth to examine whether shorter or medium length arrays minimise electrical disruption in the more distal electrodes, and comparative outcomes between MH and LW electrodes.

## Conclusion

Cochlear implantation is a safe procedure in patients with MD. Our results demonstrate that although CI in patients with MD does not trigger an activation of quiescent MD (irrespective of whether unilaterally or bilaterally performed), those with active MD pre-operatively may be at risk of requiring prolonged periods of auditory rehabilitation which may impact their quality of life. Patients with MD may achieve higher speech scores following CI when compared with non-MD patients. We emphasise the importance of pre-operative counselling to be offered to all patients with MD in order to better address expectations following surgery with reference to the likelihood of ongoing auditory rehabilitation following surgery. Evidence suggests that ablative treatment prior to cochlear implantation improves outcomes without adversely affecting speech scores. It remains unclear whether the insertion of pre-curved electrodes may facilitate re-mapping due to the utilisation of lower currents compared to lateral wall arrays.

## Declaration of interest

None

## Word count

2984

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