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Cochlear Implants as a Treatment Option for Unilateral Hearing Loss, Severe Tinnitus and Hyperacusis

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Key Words

Asymmetric hearing loss · Cochlear implant · Single-sided deafness · Sudden unilateral hearing loss · Tinnitus · Tinnitus Handicap Inventory · Visual Analogue Scale

Abstract

Tinnitus is an incapacitating condition commonly affecting cochlear implant (CI) candidates. The aim of this clinical study is to assess the long-term effects of CI treatment in patients with severe-to-profound, sensorineural, unilateral hearing loss (UHL) and incapacitating tinnitus. We performed a prospective CochlearTM company-sponsored multicentre study in five Spanish centres. Sixteen patients with UHL and incapacitating tinnitus, which was indicated by a Tinnitus Handicap Inventory (THI) score >58%, received a Nucleus[®] CI in their deaf ear. The study design includes repeated within-subject measures on hearing, tinnitus, hyperacusis and quality of life up to 12 months after initial CI fitting. In addition to hearing loss and tinnitus, all patients suffered from hyperacusis. Most patients had a sudden hearing loss and received a CI within 2 years after their hearing loss. Preliminary 6-month, post-CI activation data of 13 subjects showed that the majority of patients perceived a subjective benefit from CI treatment, which was assessed using the THI, a Visual Analogue Scale of tinnitus loudness/annoyance and the Speech, Spatial and Qualities of Hearing Scale. Preliminary 12-month data of 7 subjects showed that most patients also perceived a degree of relief from their hyperacusis. One patient showed no improvements in any of the applied scales, which could be explained by partial insertion of the electrode due to obstruction of the cochlea by otosclerosis. In conclusion, CI can success-

fully be used in the treatment of UHL patients with accompanying severe tinnitus and hyperacusis. Implantation resulted in hearing benefits and a durable relief from tinnitus and hyperacusis in the majority of patients. These findings support the hypothesis that pathophysiological mechanisms after peripheral sensorineural hearing loss are at least partly reversible when hearing is restored with a CI.

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Introduction

Tinnitus can have multiple causes [Langguth et al., 2013] and occurs in about 35% of the general population [McFadden, 1982; Axelsson and Ringdahl, 1989] and 85% of patients with hearing disorders [Coles, 1987], and the pathomechanisms underlying tinnitus and hyperacusis have often been ascribed a peripheral origin [Knipper et al., 2013]. Persistent tinnitus can have debilitating psychosocial consequences and causes psychiatric distress in 1–3% of the general population [Dobie, 2003]. Currently, there is no cure for tinnitus [Vio and Holme, 2005], and the majority of tinnitus treatment options are primarily directed towards learning to cope with the symptoms to make the patient's daily life less distressing [Noble, 2008; Cima et al., 2012; Langguth et al., 2013].

Tinnitus incidence in conventional cochlear implant (CI) candidates with bilateral hearing loss is high, ranging from 66 to 86%, while 34–93% of patients experience a durable suppression of tinnitus after restoration of hearing with a CI [Miyamoto et al., 1997; Quaranta et al., 2004; Baguley and Atlas, 2007; Tyler et al., 2008; Pan et al., 2009; Bovo et al., 2011].

Recent studies have shown that a CI can effectively restore bin-aural hearing in patients with severe-to-profound, sensorineural, unilateral hearing loss (UHL) and helps these patients to find a relief of their concomitant tinnitus [Van den Heyning et al., 2008; Kleinjung et al., 2009; Buechner et al., 2010; Carlyon et al., 2010; Masgoret Palau et al., 2010; Arndt et al., 2011; Ramos et al., 2012; Firszt et al., 2012; Gartrell et al., 2014]. Incapacitating tinnitus in an ear with single-sided deafness (SSD) can affect speech perception in noise in the contralateral ear, while a CI activating the deaf ear at threshold levels can improve the tinnitus and speech perception in noise [Mertens et al., 2013].

Tinnitus suppression primarily occurs during active CI use and is stable over time [Punte et al., 2011]. Some CI recipients experience residual inhibition of tinnitus when the implant is switched off, and these periods can extend overnight such that the recipients experiences a complete relief from their tinnitus.

The mechanisms behind the tinnitus-suppressive effects of electrical stimulation of the auditory periphery are not well understood. Acute experimental studies have shown substantial variability in the efficacy of different stimulation paradigms [Dauman et al., 1993; Rubinstein et al., 2003; Tyler et al., 2008; Di Nardo et al., 2009; Zeng et al., 2011; Chang and Zeng, 2012; Arts et al., 2015]. It has been suggested that preoperative cortical oscillations can be applied to predict CI-induced tinnitus reduction in patients with

UHL [Song et al., 2013]. The tinnitus-suppressive effect of a non-penetrating round-window single-channel implant is limited [Wenzel et al., 2014], and it has become clear that the best tinnitus-suppressive efficacy is accomplished when the full length of the CI electrode array is stimulated [Punte et al., 2013]. Hearing restoration with CI is best with multichannel intracochlear electrode arrays, and concomitant tinnitus-suppressive effects can be explained by masking effects and plastic changes in the auditory system caused by enrichment of the peripheral auditory input [Noreña and Eggermont, 2005; Eggermont, 2015].

The current literature on cochlear implants for UHL and concomitant tinnitus is based on single-centre studies. To extend the clinical experience for this emerging indication, the Cochlear™ Company is sponsoring a multicentre study in five Spanish CI centres. Investigators of these centres have shared their expertise and agreed on an extensive common protocol to investigate the clinical indications and outcomes of CI treatment for patients with UHL and an additional severe tinnitus handicap. Enrolment has been completed, and this paper reports on a preliminary data set of the study.

Subjects and Methods

Study Objective and Endpoint. The objective of this study is to show that CI treatment is effective in patients with UHL and an additional severe tinnitus handicap. The primary study endpoint is active use of the CI.

Patient Selection. Patients had to comply with the selection criteria before enrolment into the study. Inclusion criteria included age >18 years, the ear to be implanted met the local criteria for CI surgery, presence of a handicapping tinnitus, defined as score on the Tinnitus Handicap Inventory (THI) [Herráiz et al., 2001] ≥58%, normal hearing or moderate hearing loss in the contralateral ear, and failure to satisfactorily treat tinnitus with conventional treatments. Exclusion criteria included tinnitus of central origin, pulsatile tinnitus related to blood flow, paroxysmal tinnitus, somatosensory tinnitus, tinnitus related to vertigo or headache, posttraumatic tinnitus, mental disorders such as the complex regional pain syndrome, suicidal tendencies, major depression and/or personality disorders as verified by a psychologist/psychiatrist.

Study Design. The clinical investigation is designed as a prospective multicentre study with repeated measures on tinnitus, hearing and quality of life. Patients eligible for participation in the study are screened, and before CI surgery, a baseline assessment is performed, including medical history, tinnitus, hearing and quality of life. At the initial CI activation visit, the patient's tinnitus is re-assessed. Tinnitus, hearing and quality-of-life assessments are repeated at planned study visits: 1, 6 and 12 months after initial activation.

Tinnitus burden is assessed with the Spanish version of the THI [Newman et al., 1998; Herráiz et al., 2001; McCombe et al., 2001] with handicap categories for the THI score being: no handicap 0–16% (grade 1), mild handicap 18–36% (grade 2), moderate handicap 38–56% (grade 3) and severe handicap 58–100% (grade 4).

Tinnitus loudness/annoyance is assessed with a Visual Analogue Scale (VAS) ranging from 0 to 10 [Miller and Ferris, 1993]. In addition, a customised tinnitus questionnaire based on the tinnitus archive [Meikle et al., 2004] was created to fully assess tin-

nitus characteristics, history and accompanying symptoms for the study participants.

Hearing thresholds were assessed by pure-tone audiometry; speech perception was tested in quiet and in noise, and hyperacusis was assessed with the Sound Hypersensitivity Questionnaire (SHQ), known in Spain as 'Test de Hipersensibilidad al Sonido' [Herráiz et al., 2006], which was based on the German 'Geräusch-überempfindlichkeit' questionnaire [Nelting et al., 2002]. The SHQ handicap categories are: mild 1–10% (grade I), moderate 11–17% (grade II), severe 18–25% (grade III) and very severe 26–45% (grade IV).

Quality of life was assessed with the Health Utility Index Mark 3 (HUI3; <http://www.healthutilities.com/>) and quality of hearing ability was assessed with the Speech, Spatial and Qualities of Hearing Scale (SSQ) [Gatehouse and Noble, 2004].

To date, recruitment of study participants has been completed, but follow-up evaluation visits are ongoing. In this paper, we provide an overview of the demographics for the enrolled and implanted patients and their preliminary outcomes. Specifically, we present the results for the VAS, THI and SSQ scores for 13 patients assessed at the 6-month follow-up and SHQ scores of 7 patients at the 12-month follow-up. Due to the preliminary nature of the data set, selected individual and group-averaged data are presented with detailed statistical analysis preserved for the final report of the data set at completion of the study for all patients.

The study is conducted according to International Standards (ISO 14155:2011). Local ethics committee and National Competent Authority approvals were obtained before the start of the study. Patients were informed by the investigators on the risks and benefits of participating in this study, and consented before study enrolment.

Results

Sixteen patients, 8 males and 8 females, ranging in age from 31 to 70 years, were enrolled in the study. An overview of the patients' preoperative status is provided in table 1. According to the classification of the American Speech-Language-Hearing Association [Clark, 1981], all patients had severe to profound hearing loss [pure-tone average (PTA) >70 dB] in the implanted ear. In the contralateral ear, 8 patients had normal hearing (PTA <16 dB), 5 had a slight or mild hearing loss (PTA: 16–40 dB) and 3 had moderate hearing loss (PTA: 41–55 dB) aided by hearing aids. The aetiology of the hearing loss was unknown in 11 (69%) patients. In 2 patients, hearing loss was related to otosclerosis. Other aetiologies were chronic otitis, cholesteatoma/tympanoplasty and meningitis. The onset of hearing loss was sudden in the majority of patients (11/16 = 69%) and progressive in 5 (31%). The duration of sensorineural hearing loss in the implanted ear was generally short (<2 years in 12/16 = 75%) but >10 years in 2 patients. The origin of tinnitus was correlated to the hearing loss or treatment of the hearing loss. Symptoms associated with tinnitus included hearing loss, neck pain, dizziness and aural fullness. All patients had a severe tinnitus handicap (THI score ≥58%). Hyperacusis was 'very severely incapacitating' (SHQ score: 26–45) in 10 patients, 'severely incapacitating' (SHQ score: 18–25) in 2 patients and 'moderately incapacitating' (SHQ score: 11–17) in 4 patients. All patients were implanted with a Nucleus® CI, 10 received a CI24RE with Contour Advance perimodiolar electrode array and 6 a CI422 with the Slim Straight lateral-wall electrode array. Details are listed in table 1.

Fig. 1. Individual THI score for each patient obtained during a preoperative visit (Pre.) and 6 months after initial activation (6M). Patients are sorted according to the THI scale reported at 6 months. No handicap = 0–16%; mild handicap = 18–36%; moderate handicap = 38–56%; severe handicap = 58–100%.

Fig. 2. VAS results for individual patients obtained during a preoperative visit (Pre.) and 6 months after initial activation (6M) with the CI switched on and off. 0 = No tinnitus; 10 = unbearably loud tinnitus. Patients are sorted according to VAS score with the CI on. Note: no bar for '6M (CI_{on})' indicates a VAS score of '0'.

Table 1. Demographic data of the subject

Patient ID	Sex	Age, years	CI ear	CI type	PTA CI ear	PTA contralateral ear	Aetiology	Onset	Duration SNHL, years	Origin of tinnitus	Associated symptoms	THI	SHQ
11	M	48	R	CI24RE (CA)	95	20	Unknown	S	1	SNHL	Neck pain	62	31
21	F	50	L	CI24RE (CA)	120	15	Unknown	P	<1	HL	None	78	32
22	M	64	L	CI24RE (CA)	110	8	Unknown	S	13	SNHL	HL	78	31
23	F	37	R	CI24RE (CA)	92	43	Unknown	P	13	HL	HL	100	35
24	M	48	L	CI24RE (CA)	80	55	Otosclerosis	S	5	Surgery	HL	88	26
25	M	67	L	CI24RE (CA)	120	15	Unknown	S	<1	HL	HL	74	11
31	F	52	R	CI24RE (CA)	72	28	Chronic otitis	P	1	Otitis	HL	58	11
33	M	70	L	CI422	100	55	Meningitis	P	8	SNHL	HL, aural fullness, headache, neck pain	80	35
34	F	62	R	CI422	120	10	Otosclerosis	S	1	Surgery	Dizziness	76	29
35	F	48	R	CI422	115	17	Unknown	S	<1	HL	Dizziness	74	28
36	F	58	L	CI422	92	18	Cholesteatoma Tympanoplasty	P	1	Surgery	HL	74	17
41	M	40	L	CI24RE (CA)	92	20	Unknown	S	2	SNHL	HL	82	32
42	M	58	L	CI24RE (CA)	92	10	Unknown	S	<1	SNHL	HL, dizziness	70	21
43	F	31	R	CI24RE (CA)	95	5	Unknown	S	<1	SNHL	HL	62	24
82	F	51	L	CI422	120	10	Unknown	S	1	SNHL	HL	72	27
83	M	61	R	CI422	107	13	Unknown	S	1	SNHL	HL	72	17

M = Male; F = female; R = right; L = left; S = sudden; P = progressive; HL = hearing loss; SNHL = severe-to-profound, sensorineural HL; PTA (500, 1,000 and 2,000 Hz) in dB SPL. In patient 25, the electrode was partially inserted due to an intracochlear ossification identified during surgery.

Scores for the THI were obtained for 13 patients who completed their 6-month study visit. All patients reported a severe tinnitus handicap preoperatively (THI score $\geq 58\%$) and 62% (8/13) indicated a lower tinnitus handicap after 6 months of CI use. Figure 1 details the results showing that post-CI scores varied: patients 11, 22 and 31 had no remaining handicap (grade 1); patients 35, 36 and 43 a mild handicap (grade 2), and patients 24 and 41 a moderate handicap (grade 3). The remaining 5 patients (38%) showed no

reduction in the handicap grade with 2 patients (21 and 33) showing a decrease in the THI score by 20% or more.

The perceived loudness/annoyance of the tinnitus was assessed using VAS and revealed lower scores when the CI was switched on for the majority of patients, i.e. as anticipated, the reduction in VAS scores was less when the CI was switched off. Individual patient ratings are found in figure 2 with preoperative values ranging from 7 to 10. Switching the cochlear implant on resulted in a perceived reduc-

Fig. 3. Evolution of average THI and VAS scores with the CI switched on and off (n = 13).

tion in 11 of 13 patients (85%), which was indicated by a change in VAS score of 3 or more; however, 1 patient (subject 23) experienced no reduction and another indicated minimal reduction (subject 25, score changed from 10 to 9). Interestingly, at the 6-month follow-up with the CI switched off, there was no reduction or a small elevation (increase by 1) in the VAS in 7 patients (54%) while in the other 6 patients (46%) there was a decrease of 2 points or more (range 2–7).

Over time, the averaged THI and VAS scores changed in the 13 patients who completed the first 6 months of the study, with a decrease in the THI score from 75 to 56% at the initial activation and further decreases to 43% at 1 month and 42% at 6 months (fig. 3). On average, CI treatment led to a reduction of 1 THI grade. When the CI was on, tinnitus loudness (VAS score) decreased substantially from 8.4 (preoperatively) to 2.6 (at the 6-month follow-up); with the CI switched off, the effect was smaller: 6.8 at the 6-month follow-up. The effect on VAS was almost immediate at activation and remained stable over time, with a small trend to a further decrease for the CI in the on condition.

A scatter plot of both the THI percent scores and the VAS rating scores suggests a trend towards a positive correlation, e.g. preoperative data cluster in the upper right quadrant of the graph while the 6-month CI on data cluster in the lower left quadrant. VAS scores and the on/off data at 6 months as a function of the THI score of all 16 patients are included in the scatter plot in figure 4. There are outliers within the patient group, e.g. patient 42 (i.e. triangle in lower right corner; fig. 4) shows a high THI score before CI surgery and no decrease after implantation (see fig. 1 for individual data) but had a substantial reduction in the VAS score with the CI switched on (fig. 2). It can be seen that 2 patients remained within the upper right quadrant with the CI switched off, while this is also the case for 5 patients with the CI switched on.

The total scores for the SSQ questionnaire were determined before CI surgery and after 6 months in 13 patients. In 3 patients, the total SSQ score decreased, while the other 10 patients reported a perceived increase in quality of life as indicated by the higher postoperative scores (fig. 5).

Fig. 4. Scatter plot of reported VAS and THI scores of individual patients obtained preoperatively (Pre.) and at 6 months (6M).

SHQ scores before and 12 months after CI were compared in 7 patients (fig. 6). In this small group of patients, CI surgery resulted in a clear, positive effect on sound intolerance. Six of the 7 patients showed a reduction in their SHQ score. Patients 21, 23 and 41 improved from SHQ grade IV to I, patient 24 from grade IV to II and patient 31 from grade II to I, while patient 22 improved from grade IV to III. Only patient 25 showed an increase in the SHQ score from grade II to IV.

Discussion

CI have emerged as an effective treatment option for UHL in adults. Centres in Europe and America have shown that the artificial input of a CI can be integrated in a normal hearing ear and provide binaural hearing benefits while successfully reducing the burden of tinnitus during active CI use [Van de Heyning et al., 2008; Kleinjung et al., 2009; Vermeire and Van de Heyning, 2009; Buechner et al., 2010; Carlyon, 2010; Masgoret et al., 2010; Arndt et al., 2011; Arts et al., 2012; Firszt et al., 2012; Ramos et al., 2012; Gartrell et al., 2014]. Recently, children with UHL have been treated with CI [Hasepass et al., 2013], and the development of appropriate candidacy criteria will be challenging [Boyd, 2014].

Individual investigators recognise that careful selection of candidates with UHL is essential for the success of CI treatment. All patients enrolled in the current multicentre study had severe to profound, sensorineural UHL and incapacitating tinnitus, and complied with the defined inclusion and exclusion study criteria. Preliminary data show that the first 13 subjects followed for 6 months have reached the primary endpoint and are actively using their device, ranging from 8–17 h/day for 7 days a week. At the 6-month follow-up, subjects were asked to rate the efficacy of CI treatment in reducing tinnitus. On average, the group of 13 subjects reported a treatment efficacy of 79% (range 40–100%).

Preoperatively, all study subjects reported a severe tinnitus handicap (THI >58%; table 1) with a substantial decrease in the tinnitus handicap category for the majority of subjects following

Fig. 5. SSQ total scores of individual patients obtained preoperatively (Pre.) and at 6 months (6M). Patients are sorted according to relative score increases, with decreasing scores at the left and increasing scores at the right.

Fig. 6. SHQ outcomes preoperatively (Pre.) and at 12 months (12M). Hyperacusis grades: 1–10 = mildly incapacitating (grade I); 11–17 = moderately incapacitating (grade II); 18–25 = severely incapacitating (grade III); 26–45 = very severely incapacitating (grade IV).

CI surgery (fig. 1). Subjects 23, 25 and 42 had only marginal changes in their THI score; however, after 6 months, tinnitus suppression efficacy rate reported was 50, 40 and 100%, respectively. The reduction in the perceived tinnitus loudness/annoyance was highest during active CI use (i.e. CI on), with 85% of the patients showing a reduction in the VAS score (fig. 2). Patients 23 and 25 had no or only a slight reduction in VAS scores with the CI on, which is in line with their THI scores. In subject 42, there was also no effect on the THI scale, but this subject presented a 100% reduction in their VAS score with the CI on, which is consistent with their tinnitus suppression efficacy rating of 100% and potentially explains the successful use of the CI device (17 h/day). As anticipated, with the CI off, only 46% of the patients showed a reduction in the VAS score of 2 or more, and none of the patients reported a complete reduction, which is possibly related to the preoperative severity of their tinnitus.

CI surgery had minimal effects on tinnitus in subjects 23 and 25; nonetheless, subject 23 had the largest improvement in the SSQ total score after CI surgery of the group (fig. 4), which demonstrates the success of the CI treatment in this patient.

Somewhat surprisingly, the preoperative data (table 1) show that this study population scored high on the ‘Sound Intolerance Questionnaire’ with SHQ scores ranging from 11 to 35, and most subjects experienced a substantial reduction in sound intolerance according to preliminary individual data at 12 months (fig. 6). Only subject 25 experienced a substantial increase in sound intolerance after CI surgery. Based on THI, VAS, SSQ and SHQ scores, one can conclude that subject 25 had the least benefit from the CI treatment of the study group. Nevertheless, the subject reported active use of the device for 10 h/day at the 12-month follow-up. Examination of the demographic data (table 1) revealed that subject 25 had a normal contralateral ear and a sudden onset of hearing loss that was treated with a CI within 1 year, which is generally thought to have a favourable effect on treatment outcome. However, of note, the cochlear electrode array was only partially inserted in this patient due to an intracochlear ossification identi-

fied during surgery (table 1), which most likely explains the marginal changes in scores and confirms the results of an experimental study showing that full-length electrode array activation is necessary to accomplish good performance and tinnitus suppression [Punte et al., 2013].

A recent study suggested that overactivation of a hypervigilance network is involved in the greater need for treatment when tinnitus is accompanied by hyperacusis [Schecklmann et al., 2014]. Patients participating in this study presented a high preoperative tinnitus handicap (THI/VAS), which is mostly accompanied by high sound intolerance (SHQ). These patients have a clinically significant need for treatment of their incapacitating tinnitus, which possibly explains the successful daily use of the CI by all study participants, even in cases reporting limited benefits on these scales.

In mid-2015, the last enrolled subject is anticipated to complete the final study visit. At that time, the closed-study data set will be analysed and examined for potential relationships between patient characteristics and treatment outcomes as well as factors predicting CI treatment success in UHL patients. Final study outcomes may be used to support health technology assessments and future decisions of health care providers on provision and reimbursement of CI treatment in UHL cases. Furthermore, we speculate that future CI candidacy evaluation will include other hearing-related symptoms, such as tinnitus and sound intolerance. This may in turn lead to new developments in CI treatment options specifically for these symptoms. In our opinion, there is ample evidence that patients suffering from UHL with or without accompanying symptoms can effectively be treated with CI, warranting compliance by patients [Tyler, 2012] and adoption by public health care systems.

Conclusions

Preliminary data show that carefully selected UHL patients with severe tinnitus benefit from CI treatment and are actively using their device on a daily basis. Most of the study participants have

short-duration, idiopathic, sudden-onset, sensorineural hearing loss and report highly incapacitating sound intolerance. Tinnitus suppression, relief from sound intolerance and improved hearing explain to a large degree the active use of the CI in this study population.

Disclosure Statement

This paper presents preliminary outcomes of a Spanish multi-centre study sponsored by Cochlear™ Company. Authors report no conflict of interest.

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