Cochlear Implants and Hearing Preservation

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Preface

More than 10 years ago, a first experience was published by Prof. Dr. Christian Von Ilberg in preserving the low-frequency acoustic hearing while performing in the same ear a partial insertion of a multielectrode array in order to electrically stimulate mid and high frequencies. This approach was called electric acoustic stimulation (EAS).

Even with remaining good hearing at low frequencies, acoustic hearing aids are unable to adequately rehabilitate the patient at a certain stage of hearing loss and the possibility for cochlear implantation (CI) provides a solution to get better communicative abilities. Until recently patients were faced with the choice between hearing aid rehabilitation of the low-frequency hearing and CI with the loss of the remaining hearing.

The development of EAS helps to solve the traditional trade-off between being conservative and preserving the low-frequency hearing or to perform a CI and losing the remaining hearing.

The initial observation by Von Ilberg boosted basic and translational research and prompted high-technological electrode development in order to understand the fundamentals of this phenomenon and to shift this first observation to a reliable and robust procedure. Huge progress has been made to preserve, exploit, and understand low-frequency hearing and the physiology to combine and process acoustic and electric stimuli in the same cochlea.

This edition gives a state of the art from basic science to clinical application of EAS and related topics by the world leading researchers and the most clinically experienced surgical teams.

The audiological aspects related to selecting, preparing and rehabilitating EAS patients such as dead zone assessment, psychophysics of low-frequency hearing, electric-acoustic interaction, speech algorithms, music perception, fitting and acceptance by the patient are addressed in depth. Surgical minimal invasive techniques and clinical EAS results in adults and children are described in great detail.

An introductory chapter on cochlear neural reserves with exceptional images in color of spiral ganglion analysis enhances the basic understanding of the failing organ of Corti. Molecular biology with drug interference and high-technological electrode development focus further on the basic scientific EAS research.

With the development of EAS, CI has definitely put an important step ahead due to the possibility to enter the cochlea and stimulate the inner ear without destroying the cochlea and its residual hearing.

It is the primary intent of this volume to enhance the knowledge of all aspects of Cochlear implanta-
tion and hearing preservation. We also hope that the insights and experiences of the authors of this volume contribute to the understanding of the failing organ of Corti, to the benefit of classical CI and of any surgery on the inner ear.

This edition is of prime importance to every scientist, audiologist, speech therapist, and ENT specialist involved in CI and inner ear pathology.

Paul Van de Heyning
Andrea Kleine Punte
Electric Acoustic Stimulation: A New Era in Prosthetic Hearing Rehabilitation

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Abstract

Hearing preservation after cochlear implantation and combined electric acoustic stimulation (EAS) in the same ear has reduced the gap between prosthetic hearing rehabilitation with hearing aids and cochlear implants. This has increased the possibility of successful hearing rehabilitation for patients. This paper describes the history of hearing preservation after cochlear implantation. Indications and criteria for combined electric acoustic stimulation are described, and hearing preservation surgery and outcomes achieved with combined EAS are discussed. EAS has led to a new era in prosthetic hearing rehabilitation providing new understanding of basic physiological, psychoacoustic and medical aspects of the inner ear.

Inclusion criteria for electric stimulation of the auditory nerve via cochlear implantation have significantly broadened over the years. Encouraged by promising results in traditional cochlear implant (CI) patients, the application of cochlear implantation has been used in patients with increasing amounts of residual hearing. Most of these patients are able to achieve considerably good speech reception after cochlear implantation, and in some cases residual hearing could even be preserved.

Combined electric acoustic stimulation (EAS) of the auditory system is the concept of using CI technology and acoustic amplification in the same ear and is a relatively new treatment for patients with a considerable amount of residual hearing in the low-frequency range. In EAS the aim is to preserve low-frequency hearing after cochlear implantation which can be used for acoustic amplification, while a CI provides electric stimulation to the auditory system in the high-frequency range to compensate for the hearing loss in the high frequencies (fig. 1).

In 1999, von Ilberg et al. [1] first discussed the possibility of using electric and acoustic stimulation simultaneously in patients without losing functional residual hearing in the low frequencies. Evidence in animal experiments demonstrated the possibility of using electric and acoustic stimulation of the central auditory system simultaneously without interferences and the first patient with a considerable amount of residual low-frequency hearing was implanted for EAS. Long-term experience with EAS shows that preserved residual hearing after cochlear implantation remains stable over time in most patients, and encouraging results in speech reception are reported with the use of combined electric and acoustic stimulation [2–4].
**Indications and Criteria for Electric Acoustic Stimulation**

EAS is a prosthetic hearing rehabilitative treatment used in patients with normal hearing or mild to moderate hearing loss in the low frequencies up to approximately 1 kHz, sloping to a severe to profound sensorineural hearing loss in the high frequencies. These patients do not benefit much from conventional hearing aids (HAs), as HAs are efficient for mild to moderate hearing loss, while severe hearing loss in the high-frequency range (>1 kHz) is difficult to compensate for with an HA. However, traditionally cochlear implantation is not considered as a treatment for these patients with a considerable amount of residual hearing either. In figure 2, the audiogram of patients considered for EAS is shown. Maximum aided speech understanding of monosyllables should be 60% or lower. The criterion of ≤60% speech understanding is important because if residual hearing was lost after implant surgery, the amount of speech understanding using CI only would not be less than before the EAS surgery. Along with the audiogram and speech reception results, there are additional criteria for EAS candidacy: there should not be any progressive hearing loss, an autoimmune disease or hearing loss as a result of meningitis or otosclerosis or ossification of the cochlea and there should be no malformation of the cochlea. The maximum air-bone gap is 15 dB. There should also be no contraindications to use amplification devices in the EAS ear. The detection of dead regions in the cochlea could also be helpful when selecting EAS patients [Moore et al., this vol., pp. 43–50].
Hearing Preservation and Electrode Design

The success of EAS depends on the preservation of residual hearing. In order to preserve residual hearing after cochlear implantation, several EAS soft surgery techniques have been developed. The round window approach [3] and cochleostomy are most commonly used in EAS surgery. These specific surgery techniques are based on the concept of soft surgery [5] and are designed to induce as little acoustic and mechanical trauma as possible to the inner ear in order to preserve residual hearing [Adunka et al., this vol., pp. 96–107]. Special measures are taken to reduce the risk of infection and inflammation to a minimum: antibiotics are given intravenously before implant surgery, and applied locally during surgery before electrode insertion. The use of steroids diminishes inflammatory or apoptotic reactions. The operating field is also cleaned just before insertion of the electrode array into the cochlea. Although partial consensus on hearing preservation surgery is achieved, the effect and importance of some issues remain a topic of debate [Fitzgerald O’Connor and Fitzgerald O’Connor, this vol., pp. 108–115].

For a large part, a minimal invasion into the cochlea is considered to be responsible for hearing preservation. Studies in temporal bones show a significantly higher risk of cochlear trauma with deep electrode insertions of more than 360° [6–8]. When using a thinner and more flexible electrode, less force is needed when inserting the electrode into the cochlea [9]. Electrodes have been designed to be more atraumatic to the cochlea to ensure hearing preservation [Jolly et al., this vol., pp. 28–42].

Electric Acoustic Stimulation Fitting

The majority of patients implanted for EAS uses the combination of HA and CI after cochlear implantation. The acceptance of the combined use of HA and CI seems to depend on the postoperative hearing thresholds [Helbig and Baumann, this vol., pp. 81–87]. Correct fitting of the CI and HA are important to achieve the best possible speech reception results using EAS. Research has shown that CI and HA should be fitted according to the patient’s residual hearing, with a small amount of overlap between the frequency range of the HA and CI [10]. The HA should be fitted to provide an appropriate amount of amplification in the low frequencies. The half gain rule can be used for fitting of the HA. However, often more gain is needed in the low frequencies than is recommended by the fitting software. No amplification needs to be provided in the high frequencies as the patient has no functional residual hearing in the high-frequency range. Other factors that influence HA fitting are power of the HA and the amount of venting in the earmold. Electric stimulation for frequencies with hearing loss of more than 80 dB HL seems to provide

Fig. 2. Indication for EAS. Grey area indicates the range of thresholds considered for EAS treatment.
Outcomes Using Electric Acoustic Stimulation

Several studies show good results using EAS in patients with profound hearing loss in the high-frequency range [2, 4, 12; Woodson et al., this vol., pp. 125–134]. Patients using EAS have better speech reception results than traditional CI patients. Rubenstein et al. [11] also found that people with more residual hearing preoperatively tend to have better speech reception results after cochlear implantation. Even when using CI on its own, speech reception results are generally better than those of regular CI patients. The combination of CI and HA can also result in an additive or synergistic effect, providing better speech reception than with either device used alone [12]. Better speech reception in quiet and in noise might be due to better preserved hair cells and spiral ganglion cells [Rask-Andersen et al., this vol., pp. 14–27]. Compared to CI users, EAS users also perform better on music perception testing. Brockmeier et al. [this vol., pp. 70–80] show a significantly better frequency discrimination for EAS users compared to CI users, while EAS users’ scores were not significantly lower than the scores of normal-hearing listeners. The successful outcomes of EAS in adults have led to an extended use of EAS in children [13; see also Skarżyński and Lorens, this vol., pp. 135–143].

Counseling

Patients with severe sloping high-frequency hearing loss are not deaf, but often do not fit in the hearing world either. They have great difficulties with speech perception, even when fitted with HA. With low-frequency hearing and the additional help of lip reading these patients are able to ‘get by’. Often these patients have tried several HAs with limited success. Still many patients are wary of EAS surgery because they fear losing their residual hearing and becoming deaf after implantation. It is important that the risk of losing residual hearing is explained and that patients are aware that rehabilitation will take time. With reports of initial declines of speech perception after cochlear implantation preoperative counseling is important [14].

Electric Acoustic Stimulation in the Future

The rate of hearing preservation continues to increase due to improved surgical techniques as well as new developments in electrode design. An important opportunity to prevent hearing loss after EAS surgery may be in intracochlear drug treatment to protect the organ of Corti against apoptotic physiopathological pathways. Bariatt et al. [this vol., pp. 6–13] review some basic aspects of drug delivery to the inner ear in order to prevent the degeneration of the neurosensory hair cells and auditory neurons.

Research in animals could give an insight into the interactions of electric and acoustic stimulation in neural pathways [Vollmer et al., this vol., pp. 61–69] while at the same time research in EAS users contributes to a better understanding of the psychoacoustics in CI and EAS users [Gifford et al., this vol., pp. 51–60]. The benefits in speech reception and frequency discrimination when using HA and CI simultaneously in EAS patients has led to the development of new speech coding strategies in order to transfer at least some of the benefit EAS users have to regular CI users [Nopp and Polak, this vol., pp. 88–95]. With EAS an exciting new era in prosthetic hearing rehabilitation has begun.
References


Hearing Preservation in Cochlear Implantation and Drug Treatment

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Abstract
Insertion of an electrode array into the cochlea produces immediate damage to the inner ear, which is responsible for a hearing loss. In addition, delayed hearing loss can be observed. In order to maximize hearing preservation after insertion of an electrode, several strategies have been developed. Surgical techniques have been modified in order to achieve an atraumatic insertion of the electrode array into the cochlea, in particular the round window membrane approach. The electrodes were modified by manufacturers in order to avoid lesion of the cochlea. Finally, it has been proposed to infuse specific drugs into the inner ear to protect the remaining hair cells and auditory neurons from the insertion trauma. In vitro and in vivo experiments have demonstrated that it is possible to manipulate the neurosensory structures of the inner ear and provide an effective treatment to prevent the degeneration of hair cells and auditory neurons. The molecules or drugs can be administered locally to the inner ear through a direct perilymphatic perfusion or through the round window membrane. These modalities of treatment have already been successfully applied to some patients with inner ear diseases. In this paper, we will review some basic aspects of drug delivery to the inner ear to prevent the degeneration of the neurosensory hair cells and auditory neurons, and the actual applicability to humans in order to maintain hearing function after the insertion of electrodes of a cochlear implant.

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Protection of the Neurosensory Structures of the Inner Ear

Growth Factors
The function of the trophic factors in the inner ear has traditionally been thought to be promotion of the proliferation and differentiation of sensory hair cells and auditory neurons during embryogenesis. However, more recent studies suggest that the trophic factors play a much more active role in the development, polarity, homeostasis, and repair of the inner ear. Pharmacologically targeting endogenous repair mechanisms is becoming an exciting therapeutic approach.

Growth Factors in Sensory Hair Cells. Several trophic factors have been studied in an attempt to understand the development and repair of the sensory hair cells. In avian cochlea, an interesting model of self-repairing cochlea, expression of the basic fibroblast growth factor (b-FGF) and its receptor increases after injury, initiating the regenerating processes [1–3]. Bullfrog studies have suggested that b-FGF may signal hair cell survival and support cell proliferation [4]. In mammals, b-FGF belonging to the fibroblast growth factor family, a family of heparin-binding growth factors, protects injured hair cells in vitro [5] and in vivo [6]. However, this protective effect in mammals is not consistent [7]. Outer hair cell losses in the adult guinea pig organ of Corti cultures can also be prevented by treatment with several growth factors, i.e. acidic fibroblast growth factor, insulin-like growth factor 1, epidermal growth factor, transforming growth factor β1, and glial cell-derived neurotrophic factor (GDNF) [8]. In in vivo experiments, it was found that the number of surviving hair cells in GDNF-treated ears was about twice that of control ears in animals exposed to ototoxins.

Trophic Factors and Spiral Ganglion Neurons. Brain-derived neurotrophic factor (BDNF) and neurotrophin 3 (NT-3), and their receptors, tyrosine kinase B and tyrosine kinase C, provide trophic support for spiral ganglion neurons. Most neurons express both receptors, and most hair cells express both neurotrophins. These neurotrophins have been extensively used in rodents to protect injured spiral ganglion neurons [9–11]. Mice lacking both receptors, or both ligands, lose vestibular and auditory functions of the ear [12, 13]. Analyses of single mutants show distinct functions in promoting innervation by these two trophic factors (for reviews, see Agerman et al. [14] and Fritzsch et al. [15]). Mutation in genes regulating the expression of BDNF and NT-3 leads to deafness [16]. Gene therapy, by virus-mediated expression of BDNF or NT-3, rescues the spiral ganglion neurons after toxicity or trophic factor deprivation (i.e. following the loss of hair cells) [17]. Although trophic factors showed exciting results in damaged cochleas, their effect seems to be limited by the downregulation of their receptors following injury [18].

BDNF and NT-3 belong to a family of polypeptide growth factors that support survival and differentiation of neuronal populations in the cochlear and the vestibular ganglions. Tyrosine kinase receptors are structurally similar, and their ligand-induced dimerization gives rise to autophosphorylation of specific tyrosines in the activation loop of their kinase domains. Subsequent transphosphorylation of tyrosines in the juxtamembrane and C-terminal regions induces binding of different adaptor proteins that activate well-known signaling cascades like the Ras/MAPK pathway, the phosphoinositide 3-kinase/AKT pathway, and the phospholipase C/protein kinase C signaling [19].

Similarly, GDNF can prevent degeneration of auditory neurons after hair cell loss, an effect which is reinforced by electrical stimulation of the inner ear [20].

Steroids
Glucocorticoid receptors have been described within the inner ear. In the cochlea, they are expressed at the level of the stria vascularis, the organ of Corti and the spiral ganglion neurons of
the adult rat cochlea. In vitro experiments have shown that steroids have a protective effect on cultured hair cells. Tumor necrosis factor α (TNF-α), an important mediator of inflammation which is thought to be released after injury of the cochlea, induces the loss of auditory hair cells, an effect which is inhibited by dexamethasone. In addition, direct infusion of dexamethasone into the perilymphatic space has protective effects against noise-induced trauma in the guinea pig cochlea, reinforcing thus the potential role of steroids to prevent injury of the inner ear [21].

Devices Used for Local Delivery of Steroids to the Human Inner Ear

Inner ear drug delivery methods can be divided into two main categories: transtympanic and direct intracochlear infusions.

**Transtympanic Delivery**

Transtympanic drug delivery is generally accomplished by one of the following methods:
1. blind injection into the middle ear cavity through the tympanic membrane [22–24];
2. delivery through a myringotomy with a tube [25];
3. delivery with a Microwick™ placed in a myringotomy opening (Micromedics, Eagan, Minn., USA) [26, 27]. The wick is inserted through a ventilation tube which passes through the eardrum via myringotomy. Patients are able to self-administer medication. Complications include the removal of middle ear plugs or extraneous membranes prior to wick insertion, extrusion of the vent tube, and administration of topical antibiotics;
4. delivery through an implantable pump microcatheter (Round Window m-Cath™; e-cath™; Durect Corp., Cupertino, Calif., USA) [28–30]. The microcatheter has two or three lumens (one for infusion, one for fluid withdrawal and one with an electrode for monitoring ear signals). The tip of the catheter system is compressible and is designed specifically to lock in place in the round window niche;
5. stabilizing matrices.

The use of stabilizing matrices offers many potential advantages over middle ear perfusions. Medications delivered to the middle ear are ultimately dissipated by drainage down the eustachian tube or absorption by middle ear mucosa unless a stabilizing matrix is used. For potentially toxic agents, this raises significant concerns regarding isolation to target tissues. This, coupled with superior control of dosing profiles, suggests that future transtympanic delivery methodologies are likely to focus on techniques utilizing stabilizing gel matrices for passive sustained release [31]. An excellent review of several different controlled release systems is provided by Nakagawa and Ito [32]. Patterns of ototoxic damage in gerbils with sustained delivery of gentamicin using Gelfoam, hyaluronic acid, and fibrin were compared by Sheppard et al. [33] with a fibrin and Gelfoam combination found to be most effective. These approaches rely on transport through the round window membrane and result in significant basal to apical concentration gradients.

Results of treatment depend on the method of delivery. A continuous perfusion at the round window membrane is better for favorable pharmacokinetics of the drug in the perilymph [34].

**Intracochlear Delivery**

A more invasive approach with the potential for much greater control is direct intracochlear delivery of therapeutic and curative agents. This method eliminates dependence on round window membrane permeability and can provide better isolation of the delivered agent to the target tissues. A variety of tools including syringes, osmotic pumps, cochlear prosthesis-based delivery and other newer devices have been employed. Access is created via a cochleostomy through the round
window membrane or directly through the otic capsule. Intracochlear delivery of drugs or genes has been successfully accomplished in animal models by injection through the round window membrane [35].

These intracochlear techniques used in animal studies allow to develop therapeutics for humans in the future.

Local Treatment of Inner Ear Diseases

Treatment of auditory and vestibular dysfunction has become increasingly dependent on inner ear drug delivery. Recent advances in molecular therapy and nanotechnology have pushed the development of alternate delivery methodologies [31]. Current applications for inner ear drug delivery are grouped into three main categories: otoprotection, sudden sensorineural hearing loss (SSNHL), and autoimmune inner ear disease (AIED). The neurosensory cells of the cochlea must be protected from noise and surgical trauma, ototoxic drugs such as cisplatin and aminoglycoside antibiotics, and head and neck radiation. Future application research is focused on maintenance of spiral ganglion cells after hearing loss, and regeneration of hair cells. A variety of techniques including gene transfer and stem cell transplantation are being explored [36].

**Sudden Sensorineural Hearing Loss.** SSNHL is defined as the loss of more than 30 dB of hearing in three consecutive frequencies in less than 3 days [37]. Scientists still wonder about the etiology, pathophysiology and treatment of this condition. Several theories have been proposed including viral, vascular, autoimmune or mechanical etiologies. Steroids have some effectiveness in treating SSNHL, and the best indicators of treatment success are the severity of hearing loss and the time before treatment is started [36].

This disorder is an excellent candidate for local delivery. The primary reason for the use of intratympanic steroids without systemic steroids is to avoid side effects or to treat patients at greater risks for complications. The second reason is the use of local therapy after failure of a systemic treatment. The delivery of steroids to the inner ear through the round window may achieve a higher inner ear steroid concentration as compared with systemic administration [38, 39]. The Microwick, a device for facilitating diffusion through the round window membrane, has been utilized as one method of local delivery [40, 41]. In a human study of 10 patients treated intratympanically, hearing improved in 80% of participants [42]. Often, patients who have failed to tolerate systemic steroids or could not take them have been treated locally. Dexamethasone [30, 43, 44] and methylprednisolone [22–24, 28, 29, 38, 45] are the most common steroids used for intratympanic treatment of idiopathic sudden sensory hearing loss. Hearing improvement in 44–75% of patients has been reported [45]. In a retrospective study, Xenellis et al. [24] have shown a benefit in 47% of 19 patients after topical steroid therapy. Slattery et al. [22] described 55% recovery after 2 weeks of treatment of 20 patients and Herr and Marzo have [30] shown an improvement in 53% of patients treated with methylprednisolone or dexamethasone micropерfusion. Results of treatment have varied, and some studies point to a strong correlation between success and time to commencing treatment [46]. A retrospective study of a single intratympanic injection of dexamethasone showed no improvement if treatment began more than 36 days after SSNHL onset. If begun sooner, 40% of patients showed improvement [47].

**Autoimmune Inner Ear Disease (Autoimmune Sensorineural Hearing Loss).** AIED results in the loss of hearing when the immune regulation system is compromised [48]. Diagnosis of AIED is therefore based on clinical findings and on the responsiveness to steroid therapy. Immune-mediated inner ear disease (AIED) includes clinical conditions associated with unilateral or bilateral rapidly progressive forms of sensorineural hearing loss. A systemic autoimmune disorder
can be present in less than one third of the cases [49]. AIED has been reported in association with autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, Sjögren’s syndrome, polyarthritis nodosa, relapsing polychondritis, Cogan’s disease [50] and Crohn’s disease [51]. Treatment results from high-dose systemic steroids and locally delivered steroids have been inconclusive [41]. The infiltrated cells contain large numbers of TNF-α-producing cells. TNF-α is a pro-inflammatory cytokine that is secreted by activated macrophages, monocytes, T cells, B cells and fibroblasts. TNF-α induces the infiltration of immunocompetent cells into the tissues and amplifies the immune response. New pharmacologic drugs have been developed to interfere with the TNF-α signaling pathway, which was proven to be efficient in the animal model of immune-mediated labyrinthitis [52]. Encouraging results have been shown with methotrexate [53]. Ryan et al. [48] suggested a treatment using high-dose prednisone with the addition of methotrexate if relapse occurred when the steroid was tapered.

The TNF-α blocker infliximab perfused locally once weekly for 4 weeks to the inner ear allows steroid tapering, hearing improvement and relapse reduction [27]. Improvements in treatment may be facilitated by local delivery for both SSNHL and AIED.

**Aminoglycoside Ototoxicity.** Another possible application for inner ear drug delivery is in the prevention of aminoglycoside antibiotic ototoxicity due to the generation of oxygen free radicals [54]. Some reports show that the incidence of hearing loss associated with these antibiotics is as high as 33% [55]. There is a dose-dependent effect, and patients experience high-frequency hearing loss due to the loss of outer hair cells in the basal turn. Hypotheses that reactive oxygen species leading to apoptosis are involved have led to testing protective agents such as antioxidants and iron chelators [36]. The assumptions are that the antioxidants scavenge free radicals, and the iron chelators bind iron in the cochlea so it cannot react with aminoglycosides to generate reactive oxygen species [55]. A study by Sergi et al. [56] showed that antioxidants delivered with gentamicin resulted in less hearing loss.

**Cochlear Implantation and Steroids**

Insertion of an electrode array into the cochlea produces immediate damage to the inner ear, which is responsible for a hearing loss. In addition, a delayed hearing loss can be observed. In order to maximize hearing preservation after insertion of an electrode, it has been proposed to infuse corticosteroids into the cochlea. Experiments performed on guinea pig showed that local treatment of the cochlea after electrode insertion trauma with dexamethasone preserves hearing from trauma-induced loss. The local application of steroids to the inner ear is preferred because, when methylprednisolone concentrations are compared in the perilymph of the human ear and in the serum after intratympanic or intravenous administration, intratympanic administration of methylprednisolone in humans results in much higher perilymph concentrations and much lower systemic concentrations than intravenous administration [57]. In another animal study, James et al. [58] have developed a model of guinea pig cochlear implantation via a cochleostomy to study the potential protective effect of corticosteroids. Thirty minutes prior to implantation, a hyaluronic acid/carboxymethylcellulose bead, loaded with either dexamethasone or normal saline, was placed upon the round window membrane. Dexamethasone could be detected in the cochlea for 24 h after cochlear implantation. Thresholds were elevated across frequencies in all animals immediately after surgery. These thresholds recovered completely at and below 2 kHz, and partially at higher frequencies by 1 week after implantation. At 32 kHz, but not lower frequencies, the presence of dexamethasone had a significant protective effect upon hearing, which increased in magnitude over time.
The results from immediate local treatment of the cochlea with dexamethasone in an animal model of electrode insertion trauma-induced hearing loss suggest a novel therapeutic strategy for hearing conservation by attenuating the progressive hearing loss that can result from the process of electrode array insertion during cochlear implantation [59]. Interestingly, steroids and lubricants have an effect on electrical impedance and tissue response following cochlear implantation in animal models. In cats treated with dexamethasone, impedance increased to levels similar to those in nontreated cats. Impedance in triamcinolone-treated cats remained low for about 2 months after implantation, before increasing to levels similar to the other groups. Significant fibrous tissue growth was observed histologically. The results of the present study indicate that a single intracochlear application of hyaluronate or triamcinolone may postpone, but will ultimately not prevent the rise in impedance following cochlear implantation [60]. In humans, however, the application of a single dose of a steroid solution reduces the electrode impedances significantly [61]. This was confirmed by Paasche et al. [62] who investigated the effect of the intraoperative application of steroid suspension and coating of the electrode contacts with a thin film of iridium oxide on the short-term, time-dependent development of intracochlear impedance in adults implanted with the Nucleus 24 Contour electrode. Application of steroids reduced the electrode impedances, which lasted while iridium coating of the electrode contacts did not reduce the impedance significantly [62].

**Conclusion**

Delivery of pharmacological agents to the human inner ear can preserve or increase hearing after local administration. In the future, administration of these agents to cochlear implant recipients is promising to maintain the remaining hearing function, to allow electroacoustic stimulation or to enhance the performance of the implant. Several questions still remain to be answered such as the type of molecules to deliver or the infusion period. Drugs need to be chosen to target specific biochemical pathways, to promote hair cell or neuron survival or to inhibit inflammation or subsequent fibrosis of the cochlea. The period of infusion of drugs to the inner ear might be limited in time as recent animal experiment results showed a lasting effect of neurotrophin delivered to the implanted cochlea after cessation of treatment in guinea pigs [63]. These data suggest that permanent drug treatment might not be needed.

**References**


Ganglion Cell and ‘Dendrite’ Populations in Electric Acoustic Stimulation Ears

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Abstract

\textbf{Background/Aims:} The electric acoustic stimulation (EAS) technique combines electric and acoustic stimulation in the same ear and utilizes both low-frequency acoustic hearing and electric stimulation of preserved neurons. We present data of ganglion cell and dendrite populations in ears from normal individuals and those suffering from adult-onset hereditary progressive hearing loss with various degrees of residual low-frequency hearing. Some of these were potential candidates for EAS surgery. The data may give us information about the neuroanatomic situation in EAS ears.

\textbf{Methods:} Dendrites and ganglion cells were calculated and audiocytocochleograms constructed. The temporal bones were from the collection at the House Ear Institute in Los Angeles, Calif., USA. Normal human anatomy, based on surgical specimens, is presented.

\textbf{Results:} Inner and outer hair cells, supporting cells, ganglion cells and dendrites were preserved in the apical region. In the mid-frequency region, around 1 kHz, the organ of Corti with inner and outer hair cells was often conserved while in the lower basal turn, representing frequencies above 3 kHz, the organ of Corti was atrophic and replaced by thin cells. Despite loss of hair cells and lamina fibers ganglion cells were present even after 28 years of deafness.

\textbf{Conclusions:} Conditions with profound sensorineural hearing loss and preserved low-frequency hearing may have several causes and the pathology may vary accordingly. In our patients with progressive adult-onset sensorineural hearing loss (amalgamated into ‘presbyacusis’), neurons were conserved even after long duration of deafness. These spiral ganglion cells may be excellent targets for electric stimulation using the EAS technique.

The combined electric acoustic stimulation paradigm in the same ear, the so-called EAS strategy, uses both acoustic and electric stimulation of residual auditory nerve structures [1–9]. With less invasive surgical techniques and shorter electrodes the fragile inner ear structures may be conserved. Preservation of residual hearing is now a goal in cochlear implant (CI) surgery that should always aim to limit intracochlear damage. As the success rate of hearing preservation increases, patients with more residual hearing may become candidates for EAS surgery [4]. The technique was proposed already in 1994 by William House [10].

It is assumed that a key issue for a successful outcome using the EAS technique may be the neural potential in the basal part of the cochlea where the electrode lies close to the high- and mid-frequency coding neurons. How important neurons really are for the results of CI in general is still under debate [11–16]. Fewer neurons than earlier thought seem needed and if this also holds true for the EAS principle is not known. We still
know little about the way ganglion cells are stimulated within the modiolus. The neurons are located near the perilymph electrolyte and currents spread easily along the interior of the cochlea and selective stimulation within small distances using conventional monopolar stimulation seems hard to conceive. We recently identified particularly arranged connexin proteins in the human spiral ganglion [Liu and Rask-Andersen, unpubl. obs.]. Their physiological role is unknown. Are electric junctions present in a human auditory nerve and if so how can these be related to nerve synchrony and oscillations and can electric stimulation such as in EAS work in combination with acoustic hearing to replace such possible functions?

There are relatively few studies focusing on cochlear histopathology related to ears with various degrees of low-frequency hearing preservation in different conditions. Hinojosa and Marion [17] as well as Schuknecht [18] analyzed ears with profound high-tone deafness including patients with several diagnoses. Here we present data of ganglion cell and dendrite populations in ears from individuals who suffered from adult-onset hereditary progressive hearing loss with some residual low-frequency hearing. Some of these patients had low-frequency hearing making them candidates for EAS surgery. We also present information about the normal structure and innervation of the human cochlea.

Materials and Methods

Histopathology

Four female patients were analyzed with adult-onset hereditary progressive hearing loss. Their ages and years of follow-up or duration of deafness were as follows: case 1: aged 84 years, duration 3 years; case 2: aged 78 years, duration 4 years; case 3: aged 65 years, duration 28 years; case 4: aged 65 years, duration 10 years. Dendrites and ganglion cells were calculated in all 4 cases and audiocochleograms constructed according to Guild [19] and Schuknecht [20]. All had some residual hearing at low frequencies as shown by the audiograms. The temporal bones were from the collection at the House Ear Institute in Los Angeles, Calif., USA.

Transmission Electron Microscopy

Ultrastructural findings described here were in part published by Tylstedt et al. [21] and Rask-Andersen et al. [22]. Innervation of the different turns was analyzed and the spiral ganglion cells from the lower basal, upper basal, lower middle and upper middle region were sectioned separately. Montages of the ganglion area were imaged at ×1,000 and graphical reconstructions were formulated. Special attention was given to the structural relationship between the type I ganglion cells. Thin sections were viewed in a JEOL 100 SX electron microscope. The technique for scanning electron microscopy processing is described elsewhere [23]. The study was approved by the local ethics committee (No. 99398, 22/9 1999, No. C254/4, No. C45/7 2007) and patient consent was obtained.

Immunohistochemistry

The study is based on human cochleae taken out at surgery during a transtotic approach to remove a petroclival meningioma. The cochlea was dissected out and placed in 4% buffered paraformaldehyde in phosphate-buffered saline. Sections of the cochleae were embedded and rapidly frozen and cryostat sectioned at 8–10 μm. Antibodies against Cx26, 29, 30, 31, 32, 36 and 43, Trk A, B and C receptors, parvalbumin, peripherin, class III β-tubulin and neurofilament 160 were used for immunohistochemistry of the sections in combinations. Sections were subjected to the reaction to Alexa Fluor 488 and 555 (Molecular Probes)-conjugated secondary antibodies.

Confocal, Fluorescent and Bright-Field Imaging

Bright-field and fluorescent images were obtained using an inverted fluorescent microscope (Nikon TE2000, Japan) equipped with a fluorescence unit and a SPOT digital camera with three filters (for emission spectra at 358, 461, and 555 nm). For confocal microscopy, we used a Nikon TE300 microscope equipped with a laser imaging system using three different filters.

Plastic Molding of the Cochlea

In order to analyze anatomic frequency maps for short electrodes the relative length of the first turn of the human cochlea was investigated using plastic castings of 95 human inner ears. Silicone and polyester resin material was used in this investigation [24]. We used the mid-point of the long diameter of the round window as reference and starting point for measuring the length of the cochlea since we believe that round window application may be the optimal technique used in future implantations. A line was drawn through the central axis of the cochlea to a distant point of the first turn and at right angles to this line through the axis of the cochlea dividing each turn of the cochlea into quadrants.
Fig. 1. Audiocytocochleograms of cases with adult-onset progressive sensorineural deafness with various degrees of low-frequency hearing preservation. Duration of deafness varied from 3 to 28 years. For further information see Materials and Methods.
**Results**

In all 4 cases, inner hair cells, outer hair cells, supporting cells, ganglion cells and spiral lamina nerve fibers were well conserved in the apical region (fig. 1). In the upper basal and middle turn (mid-frequency region), the organ of Corti with inner and outer hair cells and lamina fibers was also generally preserved while in the lower basal turn, at areas representing frequencies above 3 kHz according to the Greenwood place/frequency map, the organ of Corti had undergone atrophy and was replaced by a thin cell layer (fig. 2). There were no lamina fibers but ganglion cells were present with a maximal loss of 60% in cases 2 and 3 (duration of deafness 4 and 28 years, respectively), and in cases 1 and 4, there was a minor loss of ganglion cells at the corresponding region (duration of deafness 3 and 10 years, respectively) (fig. 1). Light microscopy showed that spiral ganglion cells at the sites of hearing loss were often arranged in cluster and physically interacted with each other. The perikarya were surrounded by a thin satellite cell (fig. 2b, 3b inset). There were no peripheral axons emerging in the direction of the organ of Corti (fig. 3b). Central axons were myelinated and had a normal appearance. Thus, remaining type I cells were unipolar in type and most of them were located together even though a few individually sited cells were also seen (fig. 3b inset). Several free cells appeared around the neural cell bodies.

A scanning electron micrograph of a normal, optimally fixed, hemi-sectioned human cochlea corresponding to the level of section (fig. 2) can be seen in figure 4. The position of a short electrode and how it occupies the scala tympani space in the basal turn (360°) is delineated. Its relationship to the basilar membrane, organ of Corti and spiral ganglion cells can be observed (fig. 4, 5). The normal dendrite architecture with typical arborization is seen in the basal turn in an osmium-stained human specimen (fig. 5b). A graph shows the region of maximal innervation density representing the upper basal and lower middle turns (fig. 5c).

The distribution of perikarya at various locations is shown in figure 6b. Even though the perikarya are not evenly distributed along Rosenthal’s canal, it is obvious that there are normally much fewer cells appearing on radial sections in the basal region of the cochlea. From these reconstructions one can also see that perikarya often share the same satellite cells and that they often interact physically with each other, especially near the apex where the cell bodies become concentrated in a terminal bulb-like structure (fig. 6a, b). Transmission electron microscopy shows that these cells are unmyelinated and surrounded by a thin ‘satellite’ cell. Serial thin sections and 3-dimensional reconstructions of physically interacting perikarya show that junction-like specializations extend between the neuron plasmalemmas (fig. 6b). Immunofluorescence at these areas surprisingly shows an expression of Cx30 protein (fig. 6b) [unpubl. obs.]. Such an expression may be unique to humans and has not been observed in animals studied so far in our laboratory.

The human cochleae considerably varied in size and shape resulting in different insertion depths, angles and place/frequency maps of the introduced CI electrodes. The mean length of the first turn (quadrant 1–4) was 22.6 mm with a range from 20.3 to 24.3 mm, representing 53% of the total length (table 1). According to an anatomic frequency map an electrode reaching one turn approximately covers frequencies down to around 1 kHz.

**Discussion**

We found that in progressive adult-onset profound sensorineural hearing loss, with various degrees of low-frequency hearing preservation, the organ of Corti had undergone atrophy with degeneration of inner and outer hair cells in the lower basal turn. This was associated with a total
Fig. 2. Histological section of the cochlea from case 4.  

a In the lower basal turn (approx. 4 kHz area), the organ of Corti is atrophic and there are no lamina fibers (×400).  
b Spiral ganglion cells are preserved (×200).  
In the mid- and apical portions of the cochlea, the organ of Corti (c; ×400), lamina fibers and ganglion cells (d; ×200) are fairly well preserved.
Fig. 3. Histological sections of the organ of Corti at the apex (a; ×400, approx. 250 Hz) and basal turn (b; ×400, approx. 4 kHz) in a patient with progressive sensorineural hearing loss. Atrophy of the organ of Corti is associated with loss of lamina fibers but not with loss of ganglion cells (inset; ×400, 4 kHz). Stained with osmium and hematoxylin.

Fig. 4. Scanning electron microscopy (×24) of a normal human cochlea corresponding to the level of sectioning demonstrated in figure 2 (mid-modiolar section, inset right). The putative location of an EAS electrode with a tip diameter of 0.4 mm is shown (red). Circles indicate the anatomic location of the spiral ganglion (a: 1–2 kHz; b: 4 kHz; c: <1 kHz). The left inset shows the introduction of an EAS electrode through the round window.
or near-total loss of lamina fibers. The spiral ganglion cells, however, were conserved to various degrees even after 28 years of deafness. These cells may be excellent targets for EAS surgery.

Conditions with profound sensorineural hearing loss and preserved low-frequency hearing may have several causes and the pathology may vary accordingly. Our results are in accordance

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**Fig. 5.**

- **a** Plastic corrosion cast of a left human inner ear. The solid line demarcates one turn (arrow). This represents approx. 20–24 mm distance from the mid-point of the round window (RW).
- **b** Surface preparation of a normal human cochlea. The distribution of peripheral processes can be seen up to one turn (osmium tetroxide, by courtesy of B. Engström).
- **c** Graph showing innervation density of the normal human cochlea (see Spoendlin and Schrott [35]). The dashed line shows the EAS electrode reaching up to one turn. NF = nerve fibres; OHC = outer hair cell; IHC = inner hair cell.
with Hinojosa and Marion [17] who correlated the state of the acoustic ganglion with that of the organ of Corti and of the peripheral fibers in 8 patients with profound hearing loss defined as an average loss of 90 dB or greater for the hearing threshold levels at 2,000, 4,000, and 8,000 Hz only. It included diagnoses such as presbyacusis (n = 6), ototoxicity (n = 6), Ménière’s disease (n = 1) and otosclerosis (n = 1). Cochlear reconstruction demonstrated the least amount of sensorineural injury among all bones examined [25], with the highest number of cells remaining in the spiral ganglion. In a 77-year-old man with residual low-frequency hearing the audiogram revealed an advanced sensorineural hearing loss at 1,000, 2,000, 4,000, and 8,000 Hz. Ganglion cell counts were only mildly reduced in all turns. Cochlear reconstruction demonstrated total loss of the organ of Corti in the first 11 mm of the basal coil, with variable preservation of the hair cells throughout the remainder of the cochlea. Peripheral cochlear nerve fibers were also absent in the basal turn, but increased steadily into the apex.

Injury to the organ of Corti seems to result in retrograde degeneration of peripheral cochlear nerve fibers. Otte et al. [26] stated that loss of the spiral ganglion cells seems to parallel the extent of injury of supporting cells rather than of hair cells. According to studies by Spoendlin [27] based on cats, loss of inner hair cells resulted in retrograde degeneration of the cochlear neurons. Hinojosa and Marion [17], however, found that the degree of degeneration of the organ of Corti in humans including the supporting cells does not correlate with the number of remaining lamina fibers or spiral ganglion cells. They assumed that factors other than the state of the organ of Corti, supporting cells, and peripheral fibers have an effect on the extent of ganglion cell loss. Thus, contrary to what happens in animals, loss of hair cells and even loss of the entire organ of Corti does not lead to complete neuron loss. This disparity is of fundamental importance for CI as well as EAS. The reason for the slow degeneration remains puzzling. We speculated that neural perikarya may obtain local trophic supply from each other through their physical interaction. This is made possible through their lack of myelin [21, 22]. This interaction is noticeable in the apical region where even specific junctions occur between bordering cells (fig. 6b) [28, 29]. However, histology from cases 1–4 shows that some type I cells have no physical contact with each other, so this explanation cannot fully explain the degree of preservation. Interestingly, human perikarya are enclosed by a different type of cell, here named ‘satellite’ cell, that contains no myelin. Degeneration of the peripheral axons together with their myelin-containing Schwann cells starts at the periphery and may cease at the axon hillock where the ‘satellite’ cells enclose the perikaryon. Satellite cells may not be affected by the degeneration. In the situation where the peripheral axon and the cell body are myelinated, the degeneration process may also involve the cells surrounding the perikaryon. This cell is of paramount importance for the protection, function and survival of the neuron. It produces survival factors such as glial cell line-derived neurotrophic factor. We found Trk B selectively expressed on perikarya; a target for the neurotrophin brain-derived neurotrophic factor [Liu et al., 2008, unpubl. obs.]. One way to further prevent degradation of neurons could therefore be to add small amounts of these growth factors via the implant using drug delivery systems.

If preservation of peripheral processes improves electric stimulation or maintains the integrity of spiral ganglion cells is not known with certainty. Reports of animal studies have indicated that it is the cell bodies or possibly central axons that are being stimulated by the implant [30] and human implanted temporal bones suggest that performance is unrelated to the percent of remaining peripheral processes and spiral ganglion cells [16]. The degeneration of lamina fibers seems to occur more promptly following inner hair cell loss, which is thought to head fiber degeneration. This deterioration then seems to decelerate once
reaching the cell bodies. However, as stated earlier, the conditions may be highly varying and maintained lamina fibers can also be noticed despite total loss of inner hair cells [17, 31].

The apical part of the cochlea is known to be more resistant to degeneration with conservation of sensory structures. This biological principle seems to remain through animal series and may have an evolutionary background. Rosenthal’s canal is well defined only in the first turn of the human cochlea where the location of neurons matches that of innervated hair cells. More apical neurons coalesce into a less well-defined bony canal where neurons are tonotopically compressed. The spiral ganglion in humans goes only as high as the middle segment where dendrites spread out to innervate the third turn [32] (fig. 6a, b, 7). Electrodes reaching the second turn may therefore stimulate neurons coding for lower frequencies than represented by their location. This may imply that selective stimulation of neurons coding for particular frequencies is more intricate in the apical region than in the basal region. This condition may have a bearing on the EAS strategy since the use of acoustic stimulation in the low-frequency region may provide more temporal fine structure hard to obtain through electric stimulation.

The optimal length and design of the implanted electrodes as well as the most suitable surgery for the EAS patients are still a matter of debate. Different short electrodes ranging from 6–10 to 21–24 mm have been constructed [1, 2, 4, 7, 33, 34]. The original 6-mm device was lengthened to 10 mm with the most apical electrode at approximately 2,500–3,000 Hz according to the Greenwood place/frequency map. The tip of the electrode curves into the ascending segment but does not extend to the upper basal turn of the
cochlea. The most innervated region of the human cochlea is the upper basal and lower middle turns (fig. 5c) [35]. An electrode reaching one turn is close to the most densely innervated areas, which may be advantageous in case of inadvertent deafness caused by EAS surgery. We found that at one turn (approximately 1 kHz) both hair cells and lamina fibers were well preserved but apparently nonfunctional.

Cochlear inner and outer wall lengths differ greatly and an electrode runs deeper if placed against the modiolus than the outer wall. This is due to the larger diameter of the first turn and the modiolus. The large variations in cochlear anatomy may favor the idea of using more individually shaped electrodes. Since the medial wall of the cochlea is fragile it would seem imperative not to exert any physical pressure on this structure [36]. Our studies of the human cochlea show that each person’s cochlea is individually shaped [24]. Variations in size and shape result in different insertion depths, angles and place/frequency maps.
of the introduced CI electrodes (table 1). When performing CI surgery in patients intended for combined EAS it is necessary to consider these anatomic variations. Based on measurements of 65 plastic molds of the human cochlea, the first turn extended from 20.3 to 24.3 mm with an average of 22.6 mm. This represents the length of an electrode reaching one turn to approximately
1 kHz. These results are in accordance with those by Adunka et al. [34] and Gstoettner et al. [7] who found that a 360-degree insertion of the array entering this region, which defines the end of electric stimulation and beginning of acoustic stimulation, corresponds to 18–24 mm. This depth was found to provide good CI performance for both combined EAS and electric stimulation alone in case of loss of residual hearing without the need for reimplantation. A shallow insertion reduces the risk of damage to apical cochlear structures while a deep insertion of the array may improve CI performance in case residual hearing is lost. Another concern is the potential deterioration of residual low-frequency hearing over time.

EAS technologies aiming at preserving acoustic hearing and providing electric stimulation of residual ganglion cell bodies may improve esthetics of sound including speech comprehension in noise and multitalker backgrounds as well as music perception [37, 38]. In a recent study of hybrid patients, they were found to score nearly as accurately as normals for melody recognition, whereas long-electrode patients performed very poorly [39]. The question arises how many residual ganglion cells in the basal turn are necessary to provide benefits from such a strategy. Are they necessary or can neurons higher up in the cochlea compensate for their loss? How can we preoperatively assess the amount of residual ganglion cells still present in the lower turn? Humans have approximately 30,000 neurons [26, 40] and almost 50% of these are located in the first turn. At present, it is not possible to predict the neural potential of the cochlea and its different parts. Despite a profound hearing loss, we know the numbers of surviving cells may be considerable. The ganglion cell populations have been found to be largest in ears deafened by sudden deafness, Ménière’s disease, and ototoxic drugs; somewhat less in vascular occlusion, temporal bone fracture, otosclerosis, and cochlear dysplasia, and least in measles, bacterial labyrinthitis and congenital syphilis [25]. In addition, fewer ganglion cells than previously thought seem necessary to achieve useful auditory sensation from electric stimulation, even as few as 10% of the normal number [13–16]. Recent data from the FDA Iowa/Nucleus Hybrid clinical trial suggest that those with more than 35 years of severe-to-profound hearing loss above 2,000 Hz often did not do well with the added electric stimulation, telling that there were not enough viable ganglion cells in the base of the cochlea to take advantage of a 10-mm electrode [9]. However, Linthicum and Fayad [41] demonstrated a case of a woman who had a lifetime, 89 years of deafness,

| Table 1. The total length (mm) of the outer wall excluding the basal half of the round window |
|-----------------------------------------------|-----------------|------------|-----|-----|
| Outer wall length                            | Mean            | Range      | SD  | n   |
| Half diameter of the round window            | 1.1             | 0.3–1.6    | 0.21| 65  |
| First half of first turn                     | 13.5            | 12.1–15.0  | 0.73| 67  |
| First turn (quadrants 1–4)                   | 22.6            | 20.3–24.3  | 0.83| 65  |
| Second turn (quadrants 5–8)                  | 12.4            | 10.7–13.3  | 0.63| 63  |
| Third turn (quadrants 9–12)                  | 6.1             | 1.5–8.2    | 1.40| 58  |
| Total length                                 | 42.0            | 38.6–45.6  | 1.96| 58  |

SD = Standard deviation; n = number of specimens.
with no hair or supporting cells with 23,000 ganglion cells.

William House [10] already in 1994 anticipated that a rising number of patients with different kinds of sensorineural hearing loss will benefit from the ‘use of complementary assistive systems one acoustic and one electric’. We see a new era of implantation emerging. Innovative strategies are necessary to design even more sophisticated electrodes not only for saving residual hearing but also for more selective stimulation of the neural components of the human cochlea.

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References


Electrode Features for Hearing Preservation and Drug Delivery Strategies

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Abstract

Background/Aims: Reducing the risk of hearing loss after cochlear implantation requires optimization of the electrode array to minimize the physical trauma caused by insertion and placement. Furthermore, the electrode design must be optimized for atraumatic surgical approaches. Even greater levels of protection may be achieved by the use of a drug during and after implantation. The electrode array offers a potential vehicle for drug delivery. Methods: This article reviews the laboratory and clinical data available thus far relating to the importance of electrode design parameters for trauma minimization, and the possibility of further reduction through pharmaceutical intervention. Candidate drugs were identified through literature review and laboratory evaluation. The most promising have been investigated in vitro and in animal models of implantation trauma. Three delivery devices are currently under development to satisfy the specific demands of different therapy regimes. The delivery profiles of each were evaluated through both modelling and bench testing and the concepts investigated in vitro and in vivo. Results: Current evidence favours a thin, flexible electrode array with wires in a zigzag shape. Steroids and an apoptosis inhibitor (AM111) performed well in animal models of electrode trauma and are both good drug candidates for reduction of the risk of hearing loss after implantation. Semi-chronic dexamethasone elution, acute drug delivery by intracochlear catheter, and longer-term delivery through diffusion from a reservoir were all shown to be feasible. Conclusion: An extensive programme focussed on minimizing hearing loss through device optimization and the development of new technologies has yielded positive results and new concepts for further development and clinical application.

Features of Electrodes Desirable for Electric Acoustic Stimulation Surgery

It is generally assumed that to maximize the chance of hearing preservation during cochlear implant surgery an atraumatic electrode array is required and that the electrode length should be limited to reach the 1,000-Hz region, equivalent to an insertion angle of about 360°, or less. In order to reduce trauma and increase the chance of hearing preservation, the cochlear implant manufacturers offer lateral wall electrodes: from MED-EL GmbH the approved FLEX EAS [1], and a FLEX 20-mm-long prototype in testing [Helbig S., in preparation], from Cochlear Ltd. the Hybrid S [2] and Hybrid L [3], and from Advanced Bionics Corporation a ‘Thin Lateral’ and a HELIX II electrode have been...
reported [4]. Preshaped electrodes such as Contour Advance or HELIX increase the risk of hearing loss and are not designed for consistent hearing preservation due to the large number of direct scala vestibuli insertions and deviations from scala tympani to scala vestibuli [5]. Lateral wall electrodes are assumed to be less traumatic than preshaped electrodes and are preferred for hearing preservation.

Histological studies performed in fresh and fixed human temporal bones have demonstrated that electrode arrays inserted in the cochlea can cause mild to severe trauma [6, 7]. With a good electrode design the occasional trauma is limited to a spiral ligament compression and basilar membrane bulging in localized region(s) of the cochlea. The location most at risk from trauma is the point of 1st contact between the electrode and the lateral wall for free-fitting lateral wall electrodes, at an insertion angle of around 90°. With a poor electrode design the trauma can include electrode displacement from scala tympani to scala vestibuli with spiral lamina fracture and rupture or displacement of the basilar membrane, with risks of endolymph and perilymph mixing [8].

The key features to reduce electrode trauma in the cochlea are the size and flexibility of the array. The electrode should be much smaller than the dimensions of the smallest cochlea, but without compromising the pushability of the electrode. Most importantly, the electrode should be flexible to easily adapt to the angulations of the basal and second turn of the cochlea, regardless of lateral or medial wall positioning. A key feature to make an electrode flexible is zigzagging the platinum-iridium wires inside the electrode silicone carrier (fig. 1). A collection of straight wires, even 25 μm in diameter, increases the rigidity and more than doubles the insertion force of the electrode compared to an array with wires in zigzag form. Slightly reducing the diameter of the metallic wire reduces insertion forces, but not as much as wiggling the wire into zigzag shape. Measurements of the insertion force of a commercially available electrode with a network of zigzag wires (fig. 2)
are shown in figure 3 and compared to the insertion force of the same electrode with straight wires. Insertion forces were compared in the same 3-dimensional plastic 1:1 size scala tympani model. In both cases, the electrode wires were platinum-iridium 25-μm wires, Teflon insulated to a diameter of 33 μm.

The least traumatic (and surest) approach for entering the scala tympani is through the round window, after partial removal of the so-called round window niche [3, 9]. The annulus around the round window should be untouched. Entering the cochlea purely through the round window does not cause any disruption of the spiral ligament and associated bleeding from venules that irrigate the lateral wall soft tissues. A round window puncture of the size of the electrode diameter at its most basal end is required. For such a non-cochleostomy approach, the electrode diameter at its most basal end should be smaller than the width of the round window, preferably less than 1 mm in diameter. The success of the electric acoustic stimulation approach demonstrates that partial blockage of the round window by a foreign body does not significantly suppress cochlear mechanics. This fact has also been recently demonstrated by the successful placement of an implantable middle ear mechanical transducer in the round window niche [10].

With the round window approach, the point of 1st contact between the electrode tip and the lateral wall takes place sooner than with a cochleostomy approach. If the front end of the electrode (initial 10 mm) is superflexible, the electrode array has no difficulties engaging the lateral wall of the cochlea with minimal trauma. Superflexible front end electrodes have little chance of deviating from one scala to the other during insertion since the softness of the electrode associated with its flexibility preclude the possibility of developing the force necessary at the electrode tip for basilar membrane perforation or spiral lamina fracture. Contrary to rigid electrodes, superflexible lateral wall electrodes do not have a ‘tip fold-over’ when pushed into an area of increased resistance. Tip resistance to insertion causes basal buckling of a flexible electrode at or near the entrance point, be it round window or cochleostomy [11].

In order to reduce stiffness and increase electrode flexibility it is desirable to keep the channel...
density low. A large number of channels over a short length increase stiffness and subsequent risks of trans-scala displacement. Fewer contacts, spaced further apart, increases flexibility. In any case, the front end of the electrode should be especially flexible to engage well into the scala tympani without deviation of the tip. Differential contact density between the front end and the back end of the electrode array may be warranted. In one electrode design, reduction of front end wire and contact density by 50% and an associated reduction in size and volume yielded a significant reduction in insertion force [1].

Low-frequency hearing loss after hearing preservation surgery that includes the insertion of a short or medium electrode array is not directly related to the physical presence of the electrode since the hearing loss is in a region where no electrode carrier is present. Hearing loss in that case is related to the indirect effects of trauma, caused either by the electrode insertion or the surgical opening of the cochlea or a foreign body reaction such as fibrosis. The indirect effects may include inflammatory processes [12], cell necrosis and apoptosis [13], fibrosis [14], and blood diffusion [15].

It has long been assumed that the presence of an electrode near an organ of Corti region with functional hair cells would guarantee the destruction of hearing in this region. There are reports that the presence of an electrode in the low-frequency region does not always prevent hearing preservation [16, 17], just as there are reports that insertion of a very short electrode array is not a guarantee for hearing preservation in the low-frequency region [2].

The optimum electrode insertion depth for hearing preservation is unclear at this time. More prospective studies are needed. Also needed are studies that evaluate the mechanical effects of the electrode on hearing preservation in cochlear implant patients with more or less flat but measurable audiograms, or even in patients with residual high-frequency hearing. In order to better and consistently control the indirect effects that can cause hearing loss in the low-frequency region during hearing preservation surgery, a pharmaceutical strategy is necessary [18].

**Pharmaceutical Approaches for Hearing Preservation**

Experience has shown that most of the causes of postoperative hearing loss after cochlear implantation can be minimized by electrode design, and optimized surgical technique with acute attention to detail. However, the degree of variation in anatomy and underlying pathology, the required level of surgical skill and (as yet undetermined) factors after implantation leave considerable potential risk to hearing. Protection of the cochlea during implantation is likely to have benefits for most cochlear implant candidates, either through hearing preservation or through increased protection of the status of the auditory nerve. Furthermore, as greater success is achieved, audiological boundaries will be pushed, and hearing preservation will be explored with greater insertion depths and greater degrees of residual hearing. Patients with progressive hearing loss might be implanted earlier, and with a better outcome, if the remaining hearing could be maintained. The safe and appropriate development of pharmaceutical approaches for hearing preservation in cochlear implant patients is likely to be a major milestone in the practical development of pharmaceutical therapies against acquired deafness. The invasive nature of cochlear implant electrode insertion itself provides both an opportunity for accurate local drug delivery and a platform for the development of a delivery device.

Effective treatment of hearing loss using a pharmaceutical approach requires an understanding of the underlying mechanisms at the molecular level. Cochlear pathology has traditionally been difficult to analyse due to inaccessibility, size and the difficulties associated with creating models of disease.
However, a number of researchers have made significant progress in recent years in, for example, animal models of ototoxicity, noise trauma and cochlear implantation. Inflammation and cochlear homeostasis are better understood. A review of current work relating to the protection and repair of inner ear sensory cells is given in Forge and Van de Water [19]. Eshraghi and Van de Water [20] describe how cochlear implantation trauma activates both inflammatory and cell death pathways, and may involve several mechanisms at the molecular level, i.e., necrosis, necrosis-like programmed cell death (type 2 programmed cell death), and apoptosis (type 1 programmed cell death).

Two drugs shown to be very effective in animal models of implantation trauma are the apoptosis inhibitor AM111 (D-JNK-1 inhibitor), currently undergoing clinical trials against acute sensorineural hearing loss (Auris Medical, Switzerland), and steroids, including dexamethasone. Eshraghi and Van de Water [20] demonstrated apoptosis in upper turns of the guinea pig cochlea after implantation trauma and reduction in the degree of hearing loss using AM111. Staecker et al. [unpubl. data] have reported increased levels of TNF-α (an inducer of inflammation) in the cochlea after implantation trauma. Keithley et al. [21] demonstrated that TNF-α can recruit leucocytes into the cochlea at concentrations that are not cytotoxic to sensory cells in the organ of Corti. Dinh et al. [22] demonstrated in organ-specific culture that TNF-α may have a direct toxic effect on hair cells by increasing the Bax/Bcl-2 ratio. A number of groups have investigated the use of steroids (to suppress the inflammatory response) using a variety of delivery methodologies, demonstrating efficacy in the protection of hearing after mild to moderate levels of trauma [23–26] (see also the study of dexamethasone elution by Kiefer et al. [27] reported later in this article). Steroids can have quite a wide spectrum of activity, however, including antioxidant and homeostatic effects. Possible mechanisms specific to this application are reviewed in Eshraghi et al. [13] and Dinh et al. [22]. In another study, Barkdull et al. [28] demonstrated considerable efficacy of AM111 against hearing loss caused by inflammation. Both drugs therefore appear viable for further development. The suitability of a drug for use in the inner ear depends on many factors. Foremost is the issue of safety. Additionally, specific features of the drug and its formulation are important to the design of the delivery system [29]. These include molecular weight and charge, rate of clearance, time of action, adherence to the materials of the system, stability, specificity, and solubility. The ratio between effective and toxic concentrations must be high enough to allow for uncertainties in distribution, and the available formulations and regulatory status of the drug will affect the system development costs.

**Delivery Devices Tailored to the Application**

Each possible therapy identified through basic research requires a delivery system capable of adequate, and accurate, dosage to the target tissues in the required time frame. Some therapies, for example AM111, require application within a few hours. Others, such as steroids, may be most effective using delivery over a number of days or weeks, whereas targeting, for example, long-term fibrosis, or chronic or progressive pathologies, may require extended periods of treatment. The future may even allow treatment extended over many years with either slow release or periodic bolus delivery. Possible delivery mechanisms include systemic (oral or injection), round window delivery (diffusion or injection), and a number of intracochlear delivery methodologies. For many drugs it is anticipated that local delivery will be preferable, and in some cases necessary, to avoid systemic effects, reduce the usage of expensive drugs, and allow accurate local dosage. Proteins, peptides, liposomes and biologics normally require local delivery. Round window diffusion is relatively simple, but is unlikely to be optimal for the electric acoustic stimulation application. Due
to the slow rate of diffusion of substances along the scala tympani, combined with clearance from the perilymph and variability in round window membrane permeability, very high doses or extended treatment times are likely to be required for adequate treatment of the apical turns [30]. Three systems currently under development will be described in the following paragraphs.

**Elution of Dexamethasone from the Electrode Carrier**

Farahmand and colleagues (US patent publication No. 2007/0213799A1) have demonstrated that pharmaceutical grade micronized dexamethasone can, with proprietary techniques, be homogeneously mixed with the medical grade silicone elastomer used in the cochlear implant electrode array, and that the resulting combination product will elute dexamethasone into physiological media in a predictable manner. Depending on the drug percentage loading and the geometry of the eluting silicone, the release rate and duration can be predetermined according to the desired treatment regime. After an initial release burst (dependent on the device constituents and the initial surface treatment), a steady state is rapidly reached in which the rate of release is primarily determined by the surface area in contact with the fluid. The release duration is determined by the cross-sectional area of the device and by the total load of drug substance. Elution of a low dose of dexamethasone from a submillimetre silicone rod such as the implant electrode array is indeed possible for many months, if required – but shorter

**Table 1. Batch-to-batch reproducibility of some of the samples [32]**

<table>
<thead>
<tr>
<th>Drug percentage</th>
<th>Batch</th>
<th>Release amount on the first day μg</th>
<th>Release amount after 1 month μg</th>
<th>Release amount after 2 months μg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25</td>
<td>batch 1</td>
<td>0.2479</td>
<td>2.7074</td>
<td>4.4465</td>
</tr>
<tr>
<td></td>
<td>batch 2</td>
<td>0.2366</td>
<td>2.6305</td>
<td>4.4009</td>
</tr>
<tr>
<td></td>
<td>batch 3</td>
<td>0.2728</td>
<td>2.8838</td>
<td>4.7306</td>
</tr>
<tr>
<td></td>
<td>mean ± SD</td>
<td>0.25245±0.0185</td>
<td>2.7405±0.1298</td>
<td>4.5260±0.1786</td>
</tr>
<tr>
<td></td>
<td>RSD</td>
<td>7.35255</td>
<td>4.73822</td>
<td>3.94756</td>
</tr>
<tr>
<td></td>
<td>p value</td>
<td>0.35</td>
<td>0.097</td>
<td>0.102</td>
</tr>
<tr>
<td>2</td>
<td>batch 1</td>
<td>0.8149</td>
<td>10.0200</td>
<td>17.1006</td>
</tr>
<tr>
<td></td>
<td>batch 2</td>
<td>0.8711</td>
<td>10.2921</td>
<td>17.4384</td>
</tr>
<tr>
<td></td>
<td>batch 3</td>
<td>0.8712</td>
<td>10.1037</td>
<td>17.5676</td>
</tr>
<tr>
<td></td>
<td>mean ± SD</td>
<td>0.8524±0.0324</td>
<td>10.1386±0.1393</td>
<td>17.3689±0.24111</td>
</tr>
<tr>
<td></td>
<td>RSD</td>
<td>3.80810</td>
<td>1.37413</td>
<td>1.38822</td>
</tr>
<tr>
<td></td>
<td>p value</td>
<td>0.559</td>
<td>0.459</td>
<td>0.344</td>
</tr>
</tbody>
</table>

RSD = Relative standard deviation.
release times can be set by appropriate design parameters.

Dexamethasone was thoroughly mixed with two parts silicone at 0.25, 0.35, 0.5, 1.0 and 2.0% weight for weight of the final cured polymer. Three consecutive batches were prepared for each percentage loading for reproducibility analysis. For each batch and concentration, four samples of the eluting silicone were created with dimensions representative of the intracochlear portion of the electrode array, without contacts or wires, and each underwent in vivo release experiments in both sink (5 ml) and non-sink (1 ml) conditions using normal saline at 37°C as the release medium. The concentration of dexamethasone in the release medium was determined at geometrically spaced intervals using HPLC analysis. Excellent batch-to-batch reproducibility of the samples was found across the range and is illustrated in table 1, for the extremes of the range. Figure 4 shows the cumulative amount of drug released from silicone dummy electrodes of various dexamethasone loading over a 250-day release period, illustrating the dependence of daily dose on drug loading. The release profile was also strongly affected by the specific ratio of the two constituent parts of the silicone used for dummy electrode preparation. This is believed to be a direct consequence of variations in cross-link density, as shown in figure 5.

The silicone produced by this method has very similar properties to that of non-eluting silicone, except for an increase in opacity. Importantly, no change is imparted to the physical properties of the manufactured electrode array, in contrast to significant increases in stiffness typically found after ultrathin coating with drug-releasing biodegradable polymers. Clearly there are many advantages associated with such a delivery regime; the drug can be released uniformly along the electrode array, imparting a large advantage over round window delivery. The steroid-eluting electrode array can be used in the same way as a standard cochlear implant electrode, adding no time or complexity to the surgical procedure. Furthermore, the lack of additional chemical entities (i.e. drug excipients) reduces the risk of toxicity to the inner ear tissues compared to fluid-based approaches.

The optimal delivery period for anti-inflammatory agents after implantation has not been fully established, but there is evidence of efficacy...
in animal studies after delivery of a single application of dexamethasone phosphate [25] and after maintenance of a low dose of dexamethasone base for a period of 8 days [26]. Any possible benefits of extending the treatment regime beyond the first few weeks after implantation would need to be balanced against increased risks due to prolonged exposure to the drug.

Kiefer et al. [27] investigated the efficacy of dexamethasone elution in reducing hearing loss after cochleostomy and insertion of rods of implant grade silicone 3–4 mm into guinea pig cochleae. Rods of dexamethasone-eluting silicone were created, 0.6 mm in diameter, with drug loadings of 2 and 10%. In the animal model, in vivo measurements of drug concentration were made at sacrifice using apical fluid sampling of 10 μl at selected intervals after implantation of dexamethasone-eluting electrodes. The results are shown in figure 6. This figure illustrates the higher dosing achieved with higher drug loading for the same geometry. A burst release is followed by a relatively stable concentration during the first week. After this time, the rapid clearance from the cochlea combined with the small sample volume brought the concentration below the detection limit of the HPLC system. Importantly, there was no evidence of accumulation of drug in the perilymph at the doses used.

In the same model, the degree of hearing loss after implantation of eluting and control (non-eluting) silicone rods was evaluated (n = 18/group). Auditory thresholds were established using tone burst BERA and distortion product otoacoustic emissions. The data are shown in figure 7. At 1 month, there was a significantly lower threshold shift, at mid to high frequencies, after implantation with dexamethasone-eluting rods than in
animals implanted with control rods. This difference was maintained for 24 weeks.

Ongoing safety studies are now evaluating the effect of steroid elution on infection risk. Locally applied steroids are known for their ability to inhibit wound healing, and this has potential adverse effects for both hearing preservation and postoperative infection (through increase in the time for tissue sealing around the electrode array). This risk should always be borne in mind when introducing steroids to the middle ear during cochlear implant surgery, particularly due to

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**Fig. 6.** The concentration of dexamethasone measured in the guinea pig cochlea at various times after implantation of rods of dexamethasone-eluting silicone, with drug loadings of 2 and 10%.

**Fig. 7.** The degree of hearing loss (threshold shift) after implantation of eluting and control (non-eluting) silicone rods at various times after implantation (n = 18/group) using tone burst BERA. Differences between the curves were significant according to the Mann-Whitney U test at all time points.
the rare but potentially catastrophic nature of the risk involved. It is likely that such a risk will be related to the drug dosage and duration of application, in addition to the methods used for electrode array entry to the cochlea and sealing the site of cochleostomy or round window entry. The safety studies will investigate the effect of dexamethasone elution on cochleostomy sealing, and on the risk of meningitis after bacterial challenge, in animal models.

As the device described is an innovative combination product in which a medicinal product performs an ancillary function to an active implantable medical device, at a new location for drug application, the route to device approval will be complex. Comprehensive laboratory evaluation of the product will be required to include assessments of interactions of all constituents, in addition to safety evaluations around the use of dexamethasone in the inner ear. If these have a positive outcome, as anticipated, then evaluation of the finished product will be performed according to the requirements of the competent authorities through a structured programme of clinical trials, with the performance of the drug in reducing the risk of hearing loss after implantation defined as a primary endpoint.

**Intracochlear Drug Injection Prior to Electrode Insertion with a Disposable Single-Use Catheter**

Acute and topical, intraoperative pharmacological treatments of the cochlea have included the use of corticosteroids in crystal (depot) or liquid form to prevent the inflammatory process from spreading [24, 32]. A drop of solution is placed at or very near the cochleostomy site. It has been assumed previously that electrode insertion will carry the solution at some depth into the scala. The hydrodynamics associated with electrode insertion suggest the opposite: the drug, instead of being brought further into the cochlea, is expelled into the middle ear due to flushing of the perilymph out of the scala by the electrode insertion. A volume of perilymph equivalent to the volume of the electrode must be expelled to make room for the electrode. The volume of an electric acoustic stimulation electrode may be 20% of the scala tympani volume for a short insertion of 20 mm, and 40% for an insertion depth of 31 mm with an electrode of standard size.

In order to bring a defined amount of drug into the scala tympani, at a known location and at some known depth into the scala, the use of a disposable single-use catheter delivery is warranted. A prototype disposable catheter is shown in figure 8. The catheter front end is exactly the shape of the intracochlear electrode used by the hearing implants manufacturer MED-EL, with a single opening at the tip. The material is the same as for the electrode (medical grade silicone elastomer). No wires or contacts are included in the catheter, making the device particularly soft and flexible. Insertion depths of up to 20 mm are achievable without significant resistance. Six silicone ink marks are shown on the catheter, 5 mm apart. Catheter insertion up to 20 mm will displace around 7 μl of perilymph (the volume of the catheter). Injection of 10 μl of an isotonic pharmacological solution will backflush another fraction of perilymph, for a total of 17 μl, which is about half the volume of the scala tympani [33]. Electrode insertion after catheter removal will simply replace the disposable device without causing additional fluid displacement. The advantage of the single-use catheter is that a known volume of drug is delivered along the cochlea. The backflush effect ensures that the drug is distributed from the catheter tip back to the insertion point (fig. 9). Further drug diffusion into the apical region of the cochlea will occur after implantation. In situ feasibility of the procedure has been investigated and will be published. In eight temporal bones, the catheter was inserted into the cochlea and a iodine solution injected. CT scans of the temporal bones show that the injected liquid is located in the scala tympani (fig. 10). Histology has revealed no perforation of the basilar membrane after gentle injection of 10 μl of solution with a Hamilton syringe. The effects
of inserting a supersoft catheter and slowly injecting a protective isotonic drug into the cochlea to preserve the apical sensory epithelium need to be investigated in vivo. Insertion and removal of a disposable soft catheter followed by insertion of a permanent flexible electrode may not be detrimental to the cochlea if the long-term protective effect of the drug outweighs the additional catheter trauma, provided this is minimal.

**Delivery of Medicinal Products or Biologics through a Gel-Filled Reservoir in the Electrode Carrier**

A number of medicinal products proposed for inner ear use are hydrophilic (and therefore immiscible with the implant silicone), complex, unstable, or too large to diffuse rapidly throughout the cochlea for treatment of the apical tissues. Furthermore, few possess a depot facility to maintain a therapeutic dosage in the cochlea, avoiding its clearance mechanisms. To satisfy the potential need for delivery of such substances uniformly over a substantial length of the cochlea, the concept of delivery from an integral gel or fluid-filled reservoir in the body of the electrode array has been investigated both in vitro and in vivo. The concept involves a single, wide channel extending most of the length of the electrode array and (potentially) beyond the intracochlear portion by several centimetres (fig. 11). Outlets from the reservoir channel to the cochlea would be small in dimension to allow control of the rate of drug release by passive diffusion out of the gel or fluid carrier. The release location could be controlled by outlet positioning, the dosage by the concentration of drug in the reservoir, and the duration

---

**Fig. 8.** Disposable intracochlear catheter prototype. The front end of the catheter shows 6 black dots, 5 mm apart; 15–20 mm insertion depth can easily be achieved in temporal bones. Cross-sectional shape and area are the same as an electrode but without wires or contacts, making the device extremely flexible. A Luer lock allows easy attachment of a Hamilton syringe (20 ml volume).

**Fig. 9.** a The catheter after priming and 20 mm insertion into a scala tympani model. b After injection of 10 μl of contrast agent. c After removal of the catheter. Note that upon injection, the contrast agent does not immediately spread any further than the tip of the catheter, and that the contrast agent distribution is from the tip to the back of the catheter, near the scala tympani model entrance (round window or cochleostomy).
by the reservoir size. The device could be pre-filled, or loadable by the surgeon at the time of implantation through a port and septum (to prevent ingress of bacteria and extracellular fluids). The use of a viscous gel to house the drug within the reservoir would prevent drug loss by device flexion during implantation, at the same time as maintaining the electrode carrier flexibility required for trauma reduction. The drug might alternatively be added to the reservoir in powder form, for release by fluid ingress into the outlets. Nanoparticles and biologics could also be delivered in such a manner.

Initial evaluation of the concept has involved in vitro assessment of dexamethasone release profiles, and an analysis of microbial contamination of a simplified reservoir implanted for 90 days in a guinea pig model. This device was a simple tube with a single outlet at the tip, implanted up to 1 mm inside the guinea pig cochlea. Six tubes initially filled with saline or dexamethasone sodium phosphate solution (Fortecortin, Merck, Darmstadt, Germany) were explanted after 90 days, and their contents incubated within 1 of 5 agar preparations specific for bacteria most likely to be found on an implant electrode. No growth of pathogen colonies was demonstrated under these conditions. In a pilot trial, the same reservoir tubes filled with physiological saline or dexamethasone sodium phosphate were implanted for 90 days, during which time frequency-specific hearing levels were assessed using the compound action potential. The results suggested a small but significant advantage of the steroid at

Fig. 10. CT scan of a human temporal bone after injection of 10 μl of iodine contrast agent within the scala. The contrast agent is distributed in the scala tympani showing no dispersion into the scala vestibuli or media.

Fig. 11. Cochlear implant with drug reservoir incorporated within the lead. The electrode lead includes an 18-μl reservoir in parallel with the wires along the major length of the electrode lead. A silicone septum at the stimulator (upper left side of the implant) allows safe priming of the reservoir prior to electrode insertion. Micro-outlets along the front end of the electrode array (showed magnified on the bottom part of the picture) allow drug diffusion within the scala tympani.
Fig. 12. Hearing threshold shifts assessed using the compound action potential (CAP) at various intervals after implantation (in guinea pigs) of reservoir tubes filled with physiological saline or dexamethasone sodium phosphate. For clarity the frequency-specific shifts are amalgamated into three frequency groups by taking the average shift over the frequencies contained in the group. The error bars represent one standard deviation. For the saline group: \( n = 6 \) (day 14 \( n = 5 \), day 90 \( n = 4 \)); for the dexamethasone group: \( n = 4 \) (day 3 \( n = 3 \), day 90 \( n = 2 \)).

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Detection of Dead Regions in the Cochlea: Relevance for Combined Electric and Acoustic Stimulation

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Abstract
A dead region is a region in the cochlea where the inner hair cells and/or the auditory neurones are functioning very poorly, if at all. People who are being considered for a combination of a cochlear implant and a hearing aid typically have a dead region in the parts of the cochlea that normally respond to medium and high frequencies, but have some functional hearing at lower frequencies. For such people, it may be useful to determine the edge frequency, \( f_e \), of any dead region. This may be relevant to choosing the most appropriate insertion depth of the electrode array, and to the way that frequencies in the input signal are mapped to acoustic and electric stimulation. It may also be helpful in interpreting the results of research studies. This paper reviews methods for diagnosing dead regions and defining the value of \( f_e \). It is argued that the value of \( f_e \) cannot be determined reliably from the audiogram, although a dead region is likely to be present at a given frequency when the hearing loss at that frequency is 70 dB or more. When a sinusoidal signal is reported as sounding highly distorted or noise-like, a dead region may be present at the signal frequency, but again this is not a reliable indicator. The TEN test is a simple clinical method for diagnosis of dead regions. Where this test gives a positive diagnosis, it is recommended that psycho-physical tuning curves be measured to define the value of \( f_e \) more precisely.

Using a frequency-to-place map [2–4], the boundary of a dead region can be defined in terms of the characteristic frequency of the inner hair cells and/or neurones immediately adjacent to a dead region. This is referred to as the edge frequency, \( f_e \) [5, 6]. A dead region may have two edge frequencies, an upper one and a lower one. However, candidates for cochlear implants typically have a dead region that starts at \( f_e \) and
extends upwards from there. In other words, the dead region extends over the middle and basal regions of the cochlea. Psycho-acoustic tests for diagnosing dead regions typically lead to an estimate of the value of $f_e$.

**Relevance of Dead Regions for Combined Electric and Acoustic Stimulation**

Many people who are candidates for a cochlear implant have some residual hearing at low frequencies. Such people may benefit from combined electric and acoustic stimulation, whereby a cochlear implant is used to stimulate the middle and basal parts of the cochlea and an acoustic hearing aid is used to stimulate the apical part of the cochlea. The acoustic aid may be used either in the same ear as the implant, or in the opposite ear [7, 8]. The determination of the presence and extent of dead regions may be useful in such cases for the following purposes:

1. To guide the surgeon in the decision as to how deeply the electrode array should be inserted, or in choosing a ‘short’ or normal electrode array [9]. This is mainly relevant for cases where the hearing aid is to be used on the same side as the implant. If a person has a dead region with a relatively high value of $f_e$, say, 1,000 Hz, the residual hearing might be of considerable use, and it would be important to try to preserve this hearing as far as possible. This might indicate the need for a shallow insertion. On the other hand, if a person has a dead region with a relatively low value of $f_e$, say, 100 Hz, the residual hearing might be of minimal use, and preservation of residual hearing may be less important. In any case, a low value of $f_e$ may indicate that the electrode can be inserted quite deeply without producing significant damage to residual hearing.

2. In tailoring signal processing to suit the individual. Usually, the cochlear implant is used to provide information about medium and high frequencies in the input signal, while the hearing aid is used to provide information about low frequencies. However, the optimal allocation of frequencies to stimulation mode (acoustic or electric) has not been established, and may well vary across individuals. If a person has a dead region with a relatively high value of $f_e$, it may be advantageous to allocate relatively more information to the hearing aid (i.e., to allocate a wider frequency range to the hearing aid) than would be the case for a person with a low value of $f_e$. Further research is needed to determine whether this is, in fact, the case.

3. To help in interpreting research outcomes for patients with combined electric and acoustic stimulation, especially in assessing whether the benefit of adding acoustic stimulation to electric stimulation is related to the value of $f_e$.

**Diagnosis of Dead Regions**

**The Audiogram**

Vinay and Moore [10] and Aazh and Moore [11] used the TEN(HL) test [12] as a method for diagnosing dead regions, and this test is described below. They showed that it was not possible to achieve both high sensitivity and high specificity when attempting to predict the presence/absence of a dead region from the audiogram. However, Vinay and Moore [10], using a sample of 317 subjects (592 ears) with sensorineural hearing loss, showed that, for each test frequency from 500 to 4,000 Hz, 59% or more of ears had a dead region when the absolute threshold was above 70 dB HL. Thus, a hearing loss of 70 dB or more is suggestive of a dead region. However, a dead region can be present at a given test frequency when the audimetric threshold at that frequency is 55 dB or less [10, 13, 14], while a dead region may be absent when the hearing loss is 85 dB or more [10, 13]. Thus, there is a large range of uncertainty. A very steep slope of the audiogram, with thresholds worsening rapidly with increasing frequency, is suggestive of a high-frequency dead region.
but does not provide a reliable diagnostic method [10, 15].

Reports of Noisy or Distorted Percepts

Hearing-impaired people sometimes report that a sinusoidal tone sounds distorted or noise-like. Several researchers have suggested that such a percept may occur when the tone frequency falls within a dead region [16–20]. Huss and Moore [21] investigated whether percepts of this type provide a reliable indication that the signal frequency falls in a dead region. Hearing-impaired and normally hearing subjects were asked to rate pure tones with a wide range of frequencies and levels on a scale from 1 to 7, where 1 indicated ‘clear tone’ and 7 indicated ‘noise’. A white noise was presented as a reference for a sound that should be rated as 7. The hearing-impaired subjects were diagnosed as having dead regions using the TEN test and using psychophysical tuning curves (PTCs; see below). The noisiness ratings were, on average, higher for the hearing-impaired than for the normally hearing subjects. For the former, the ratings were not markedly different for tones with frequencies just above or below \( f_e \). This finding indicates that judgement of a tone as sounding noise-like does not reliably indicate that the tone frequency falls in a dead region. However, ratings always exceeded 3, indicating somewhat noise-like percepts, for tones falling more than 1.5 octaves above \( f_e \). Thus, if a person reports a noise-like percept for a pure tone signal, this may be taken as indicating the possibility that the tone frequency falls well inside a dead region.

The TEN Test

The TEN test was developed as a simple and quick method for diagnosing dead regions in the clinic [12, 13]. The test involves measuring the threshold for detecting a pure tone presented in a background noise called ‘threshold-equalizing noise’ (TEN). The noise spectrum is shaped in such a way that the threshold for detecting a pure tone in the noise is approximately the same over a wide range of tone frequencies, for people with normal hearing. The masked threshold is approximately equal to the nominal level of the noise, specified as the level in a 132-Hz wide band centred at 1,000 Hz. The value of 132 Hz corresponds to the equivalent rectangular bandwidth of the auditory filter, as determined using young, normally hearing listeners, which is denoted ERBn [22]. When the pure tone signal frequency falls in a dead region, the signal will only be detected when it produces sufficient basilar membrane vibration at a remote region in the cochlea where there are surviving inner hair cells and neurones. Because of the tuning of the basilar membrane, the amount of vibration at this remote region will be less than in the dead region, and so the noise will be very effective in masking it. Thus, the signal threshold is expected to be markedly higher than normal. A masked threshold that is 10 dB higher than normal is taken as indicating a dead region [12, 13]. For a positive diagnosis, the masked threshold of the signal in the TEN is also required to be 10 dB or more above the absolute threshold, i.e., the TEN must produce at least 10 dB of masking. The test stimuli (the TEN and the sinusoidal signals) are recorded on the two channels of a compact disc (CD) and are replayed via a two-channel audiometer when the test is conducted.

In the first version of the TEN test [13], all levels were calibrated in dB SPL; this version is referred to as the TEN(SPL) test. The use of levels in dB SPL was inconvenient for the clinician, as it meant that absolute thresholds had to be measured twice, once with levels specified in dB HL when measuring the audiogram, and once with levels specified in dB SPL when conducting the TEN test. In a later version of the test [12], all levels were calibrated in dB HL; this version is referred to as the TEN(HL) test. For this version of the test, absolute thresholds measured using the test tones from the TEN(HL) CD were very similar to absolute thresholds measured using the test tones generated by the audiometer. This removed the need to measure absolute thresholds.
twice. To achieve levels calibrated in HL, it was necessary to make the levels of the test tones recorded on the CD vary with frequency, so as to compensate for two factors: (1) variations in the ‘normal’ absolute threshold with frequency; (2) variations in the output of the audiometric headphone with frequency. The recorded level was increased (boosted) for frequencies where absolute thresholds were higher or the headphone output was lower. A similar frequency-dependent boost was applied to the TEN. Since the normal absolute threshold increases for frequencies below 500 Hz and above 5,000 Hz, and the output of several commonly used audiometric headphones decreases for frequencies below 500 Hz and above 5,000 Hz, it would have been necessary to apply rather large boosts to the recorded tones and noise for very low and high frequencies. To avoid this, the TEN(HL) test was restricted to test frequencies from 500 to 4,000 Hz, whereas the TEN(SPL) test could be used over the frequency range 250–10,000 Hz.

For people who might be candidates for combined electric and acoustic stimulation, it is useful to be able to apply the test for frequencies below 500 Hz. This means that the TEN(SPL) test should be used, rather than the TEN(HL) test. However, the original version of the TEN(SPL) test only included two test frequencies below 1,000 Hz: 250 and 500 Hz. These frequencies are rather coarsely spaced. For that reason, we have developed a new version of the TEN(SPL) test that includes test frequencies of 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750 and 800 Hz. As well as including extra test frequencies, the noise spectrum has been slightly modified so that, for people with normal hearing, the masked threshold varies even less with test frequency than for the original TEN(SPL) test. We refer to the new test as the TEN(SPL)-LF test. We are currently comparing results from the TEN(SPL)-LF test with those obtained with PTCs (see below), using subjects with extensive dead regions, to assess whether the criteria for diagnosing a dead region using the test need to be modified from those used at higher frequencies.

One drawback of the TEN test is that it does not give a precise estimate of the value of \( f_e \). If the criteria for diagnosis of a dead region are not met at a given test frequency but are met at the next higher test frequency, this suggests that the value of \( f_e \) lies somewhere between the two test frequencies. Thus the precision in estimating the value of \( f_e \) depends on the spacing of the test frequencies that are used. Also, the criteria for positive diagnosis of a dead region may not be met when the test frequency falls only a little above \( f_e \). Thus, in general, it is desirable to confirm the results of the TEN test, and to estimate the value of \( f_e \) more precisely, using another method. The recommended method is by the measurement of PTCs, as described in the next section.

**Psychophysical Tuning Curves**

The ‘gold standard’ for detecting dead regions is the PTC. To measure a PTC, the sinusoidal signal is fixed in level, usually at a low sensation level (SL), such as 10 dB SL. The masker is either a sinusoid or a narrowband noise. The masker level required just to mask the signal is measured as a function of masker centre frequency [23, 24]. For normally hearing subjects, the tip of the PTC (the frequency at which the masker level is lowest) usually lies close to the signal frequency [23–27]. In other words, the masker is most effective when its centre frequency is equal to the signal frequency. However, when hearing-impaired listeners are tested, PTCs have sometimes been found whose tips are shifted well away from the signal frequency [13, 16, 28–34]. This happens when the signal frequency falls in a dead region. The masker is most effective when its centre frequency coincides with the characteristic frequency at which the signal is being detected (via off-place listening). Thus, it seems reasonable to assume that the tip of the PTC falls at the boundary of the dead region, i.e. at \( f_e \).
There are several problems associated with the measurement of PTCs. The first is that the results may be affected by the detection of combination tones produced by the interaction of the signal and masker [31, 33]. This can happen especially for a person whose hearing at low frequencies is much better than at high frequencies. If the masker and the signal both fall in a region of hearing loss, they may interact to produce a simple difference tone which falls in a region of better hearing. This difference tone may be heard even when the signal itself is masked. To avoid this problem, Kluk and Moore [33] recommended adding a fixed low-pass noise to the main narrowband masker. The noise level is chosen so that it does not mask the signal, but it does mask any combination tone produced by the interaction of the signal and the masker. A second problem with PTCs is that the results can be influenced by the detection of beats between the signal and the masker, even when the masker is a narrowband noise [31, 33]. To avoid this problem, Kluk and Moore [33] recommended the use of a relatively wide noise bandwidth, such as 300 Hz. However, the use of such a wide bandwidth is problematic for low signal frequencies, where the normal auditory filters are relatively narrow [35]. When the noise bandwidth is larger than the auditory filter bandwidth, this can result in a broadening of the tip of the PTC, making it more difficult to determine the exact frequency at the tip. For low frequencies, a bandwidth of 160 Hz may be a good compromise. If precautions are not taken to prevent beats and combination tones from being used as a cue, PTCs with two or even three tips may occur, which makes the interpretation of the results very difficult [27, 32, 33, 36].

A practical problem for clinical applications is that the measurement of PTCs can be time consuming. The traditional method of measuring PTCs is to use an adaptive forced-choice procedure to measure the masker level required for threshold for several masker frequencies. Depending on how many masker frequencies are used, it can take between 30 min and several hours to measure a PTC for a single signal frequency. A faster method is to use a masker that slowly sweeps in frequency, using a method resembling Békésy tracking to adjust the masker level so that it varies on either side of the masker level required for threshold [32, 37, 38]. The fast PTC method described by Sek et al. [38] requires about 3 min to measure a PTC. However, subjects may require a few practice runs before they give stable results [34].

The method described by Sek et al. [38] required specialized equipment. However, a version of the method that can be run on any PC with a good-quality sound card is under development and should be available soon. The masker bandwidth can be set to any desired value, and the lower and upper end of the range over which the masker frequency sweeps can also be selected. Figure 1 shows examples of PTCs obtained using the new method. The 800-Hz signal was presented at 86 dB SPL, which was 10 dB above the absolute threshold. The signal was pulsed on and off (200 ms on, 200 ms off), while the masker was continuous; this helps to focus attention on the signal, and to help the subject distinguish the signal from the masker. The masker bandwidth was 160 Hz. For the PTC in the upper panel, the masker frequency was swept from 400 to 1,200 Hz over a duration of 180 s (forward sweep). For the PTC in the lower panel, the masker frequency was swept from 1,200 to 400 Hz over the same duration (reverse sweep). The masker level was changed at a rate of 1 dB/s. The jagged dashed lines show the masker levels visited. The smoother continuous lines are plotted through the means of successive pairs of turning points. For both PTCs, the tip is clearly shifted below the signal frequency of 800 Hz. The tip frequency was about 665 Hz for the forward sweep and 595 Hz for the reverse sweep. It is common for the tip frequency to be slightly higher for a forward than for a reverse sweep [38], and the ‘true’ tip frequency can be estimated as the mean of the tip frequencies for the two cases. Thus, the results suggest that the subject had a dead region with $f_c = 630$ Hz.
General Recommendations for the Diagnosis of Dead Regions in Candidates for Combined Electric and Acoustic Stimulation

The audiogram can be used to provide an indication of the frequency at which a dead region might start. As described above, a dead region is likely to be present at a given frequency when the hearing loss is 70 dB or more at that frequency. The TEN test, especially the TEN(SPL)-LF test, is useful for initial diagnosis of a dead region. It is not necessary to perform the TEN test for every possible test frequency. It is useful to perform the TEN test for frequencies where the hearing loss is 70 dB or more, and in the case of a hearing loss that increases with increasing frequency, for one or two lower frequencies (since a dead region may start at a frequency where the hearing loss is relatively mild). Generally, the TEN test should be performed over the frequency range where the hearing loss is increasing rapidly. As noted earlier, positive diagnosis of a dead region requires that the TEN produces at least 10 dB of masking. This can usually be ensured by setting the TEN level, in dB/ERBn, to be 10 dB above the absolute threshold at the test frequency. For example, if the absolute threshold, as measured using the test tone from the TEN-test CD, is 65 dB SPL, then the TEN level should be set to 75 dB SPL/ERBn. A masked threshold of 85 dB SPL or more would then be indicative of a dead region. If the required noise level is found to be uncomfortably loud, then it should be sufficient to set the TEN level equal to the absolute threshold at the test frequency.

If the TEN test results indicate that a dead region is present, then it is worthwhile to measure PTCs for one or more signal frequencies, using the fast method, to confirm the diagnosis and to

![Diagram of PTCs](image-url)
give a more precise indication of the value of $f_e$. To obtain a PTC with a tip that is clearly shifted below the signal frequency, it is desirable to select a signal frequency that falls well inside the dead region, i.e., well above $f_e$, subject to the constraint that this should not require an excessive signal level (levels above about 90 dB SPL should probably be avoided). When it is expected that the tip of the PTC will be shifted downwards, the range over which the masker frequency sweeps should be selected to extend from well below the signal frequency (say from 0.4 times the signal frequency) to about 10% above the signal frequency.

**Acknowledgments**

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**References**


Psychophysical Properties of Low-Frequency Hearing: Implications for Perceiving Speech and Music via Electric and Acoustic Stimulation

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\section*{Abstract}
We have investigated the psychophysical properties of low-frequency hearing, both before and after implantation, to see if we can account for the benefit to speech understanding and melody recognition of adding acoustic stimulation to electric stimulation. In this paper, we review our work and the work of others and describe preliminary results not previously published. We show (a) that it is possible to preserve normal or near-normal non-linear cochlear processing in the implanted ear following electric and acoustic stimulation surgery – though this is not the typical outcome; (b) that although low-frequency frequency selectivity is generally disrupted following implantation, some degree of frequency selectivity can be preserved, and (c) that neither nonlinear cochlear processing nor frequency selectivity in the acoustic hearing ear is correlated with the gain in speech understanding afforded by combined electric and acoustic stimulation. In another set of experiments, we show that the value of preserving hearing in the implanted ear is best seen in complex listening environments in which binaural cues can play a role in perception.

Combined electric and acoustic stimulation (EAS) of the same cochlea can occur when acoustic hearing is preserved following insertion of an electrode array. Multiple studies have documented, for most patients, the preservation of low-frequency thresholds following electrode insertions of 10–20 mm. On average, mean thresholds at 125–500 Hz are within 10–20 dB of preinsertion levels depending on the electrode array and the nature of the surgical technique [1–10]. Successful hearing preservation surgery allows electric stimulation of basal neural tissue and acoustic stimulation of apical hair cells that transmit low-frequency acoustic information [1–6, 9–12]. EAS has been shown to improve speech understanding in quiet and in noise beyond that achieved by aided acoustic hearing alone or electric hearing alone [2, 3, 6, 8, 9, 13, 14]. Performance in the EAS condition is commonly much higher than the linear sum of the scores in the electric-only condition and in the acoustic-only condition.

Over a period of several years, we have investigated the psychophysical properties of low-frequency hearing, both before and after implantation, to see if we can account for the benefit to speech understanding and melody recognition of adding acoustic stimulation to electric stimulation. In this paper we (a) review our work and the work of others and (b) describe preliminary results not previously published.
Auditory Thresholds

To date, the only commonly used measure of auditory function before and after surgery has been the audiogram. Unfortunately, the audiogram does not predict the benefit gained from adding acoustic to electric stimulation in the same ear [10, 15] or in different ears [16, 17]. Additionally, a number of researchers have shown that patients with comparable ranges and degrees of residual low-frequency hearing do not enjoy comparable benefit from EAS [10, 18]. These data suggest that the pure-tone audiogram may not be the most useful tool for identifying listeners who could benefit the most from adding acoustic to electric stimulation. Motivated by this logic, we have exploited measures of auditory processing beyond tonal detection, i.e., measures of nonlinear cochlear processing and frequency selectivity, to determine whether those measures will assist us in understanding the synergisms associated with EAS.

Nonlinear Cochlear Processing

It is well known that the basilar membrane response in a healthy cochlea is highly compressive with a slope of 0.2 dB/dB. This translates to a 2-dB increase in basilar membrane output for every 10-dB increase in signal input – or a 5:1 compression ratio. This high degree of compression allows for a broad dynamic range of over 120 dB for the healthy cochlea. This compressive function is due to the electromotile properties of healthy outer hair cells which are known to enhance basilar membrane movement yielding a compressive nonlinear system. A number of recent studies have examined whether the degree of basilar membrane compression is equivalent along the length of the cochlear partition. Behavioral estimates of nonlinear cochlear function using psychophysical masking have shown similar estimates of compression at both low (250 Hz) and high (4,000 Hz) frequencies [19, 20].

Gifford et al. [15] examined whether it was possible to preserve nonlinear cochlear function following hearing preservation surgery for 6 recipients of the 20-mm MED-EL EAS array and for 7 recipients of the 10-mm Nucleus Hybrid array. Nonlinear cochlear processing was evaluated at signal frequencies of 250 and 500 Hz using Schroeder phase maskers [19, 22, 23] with various indices of masker phase curvature. We found that is it possible, but not common, to preserve normal nonlinear processing in the apical cochlea following the surgical insertion of electrode arrays 10 and 20 mm into the scala tympani. Only one subject exhibited completely normal nonlinear cochlear function postoperatively at 250 Hz. However, most subjects had some residual nonlinearity (more so at 250 than 500 Hz). Thus, most patients will enjoy some of the benefits of nonlinear cochlear function at low frequencies following hearing preservation surgery.

Nonlinear Auditory Function and Speech Understanding with Electric and Acoustic Stimulation

In the same study we found that variations in nonlinear cochlear processing did not predict the gain in speech understanding for EAS patients when
acoustic stimulation was added to electric stimulation. That is to say, patients with no evidence of nonlinear cochlear processing showed as much benefit in speech recognition when acoustic stimulation was added to electric stimulation as patients with normal, or near-normal, nonlinear cochlear processing.

**A Sensitive Test for Cochlear Damage following Surgery**

Although the Schroeder masking functions used by Gifford et al. [15] did not provide insight into the speech perception benefit gained when acoustic stimulation was added to electric stimulation, the masking functions were a very sensitive measure of damage following insertion of the electrode array. For 5 out of 13 subjects, there was no significant change in low-frequency audiometric thresholds following surgery. These same subjects, however, demonstrated considerable reduction in the degree of nonlinear cochlear processing. Thus, Schroeder phase masking is a very sensitive index of surgically related damage to the cochlea and may be the most appropriate tool to evaluate the success of ‘soft surgery’ for hearing preservation.

**Frequency Selectivity**

We have obtained estimates of frequency resolution at 500 Hz both before and after implantation for 5 EAS patients. Two subjects were implanted with the MED-EL 20-mm array and 3 subjects were implanted with the Nucleus Hybrid 10-mm array. Mean age was 43.6 years with a range of 34–71 years. In addition to the 5 EAS subjects, we obtained estimates of frequency selectivity for 15 listeners with normal hearing. The mean age of the normal-hearing group was 25.1 years with a range of 21–31 years.

Estimates of frequency selectivity were obtained by deriving auditory filter (AF) shapes using the notched-noise method [24] in a simultaneous-masking paradigm. Each band of noise (0.4 times the signal frequency) was placed symmetrically or asymmetrically around the 500-Hz signal [25]. The signal was fixed at a level of 10 dB SL, and the masker level was varied adaptively. The masker and signal were 400 and 200 ms in duration, respectively. Prior to obtaining masked thresholds, quiet thresholds were measured for a 200-ms, 500-Hz signal. All thresholds were obtained using a 2-down, 1-up tracking rule to track 70.7% correct performance on the psychometric function [26]. A 3-interval forced-choice paradigm was used for all testing.

The masked thresholds in the presence of the different notched-noise conditions were utilized to derive filter shapes using a roex \((p, k)\) model [27]. AF shapes are shown in figure 1 for each subject in the pre- and postimplant condition as well as the mean for the normal-hearing listeners. Comparisons across subjects and test points were made in terms of equivalent rectangular bandwidth (ERB) [28] of the AF. Table 1 provides the pre- and postimplant estimates of both psychophysical thresholds at 500 Hz as well as the ERB at 500 Hz. As seen in previous studies with hearing-impaired listeners, the EAS subjects demonstrated considerable intersubject variation in AF width [29, 30]. Two of the subjects (EAS4 and EAS5) demonstrated normal or near-normal frequency selectivity preoperatively – though the dynamic range of the filter was considerably less than normal for EAS4 (fig. 1). All subjects, however, displayed wider than normal AFs postoperatively (table 1; fig. 1). Two subjects, EAS3 and EAS4, demonstrated a complete lack of frequency selectivity postoperatively – with EAS3 demonstrating no frequency selectivity preoperatively, as well.

Statistical analysis using a one-way ANOVA on ranks revealed a significant difference in the width of the ERB (in Hz) between the normal-hearing and preoperative EAS subjects \((H = 8.05, p = 0.005)\). Thus even prior to surgery the EAS
patients had significantly poorer-than-normal frequency selectivity – as would be expected given the patients’ elevated auditory thresholds. A comparison of pre- and postimplant frequency selectivity did not reveal a significant difference in the width of the AF (in Hz) \((F = 1.8, p = 0.25)\). This was likely influenced by the small sample size and the fact that subject EAS3 did not have any measurable frequency selectivity either pre- or postoperatively and thus no change in the width of the AF. Nonetheless, it appears that for some patients frequency selectivity is minimally altered following successful hearing preservation surgery.

**Frequency Selectivity and Speech Understanding with Electric and Acoustic Stimulation**

The finding that frequency selectivity was poorer than normal, but still present, in some patients is consistent with the finding of Gifford et al. [15] of a diminished, but present, cochlear nonlinearity.

![AF shapes for the 5 individual EAS patients (EAS1–EAS5) and the average for the normal-hearing listeners (NH AVG). AF shapes for the pre- and postimplant conditions are represented by dashed and solid lines, respectively. The mean AF shape for the normal-hearing listeners is represented by the bold line in each panel. Subject EAS3 demonstrated no frequency selectivity either before or after implantation and thus her filter shapes are represented by superimposed horizontal lines.](image-url)
following surgery. And, consistent with the ob-
servations regarding the cochlear nonlinearity,
we did not find a significant relationship between
AF width and the gain in speech understanding
when acoustic stimulation was added to electric
stimulation for our initial 5 subjects tested.

In sum, our psychoacoustic tests document
that normal nonlinear cochlear function, e.g.
sharp frequency tuning, in the region of low fre-
quency hearing is not necessary for patients to en-
joy large benefits in speech understanding when
electric and acoustic stimulation are combined.

**Table 1.** Psychophysical thresholds for 500 Hz and estimates of ERB (in Hz) for the derived AF shapes for the subjects
with normal hearing (NH) as well as the pre- and postimplant EAS subjects

<table>
<thead>
<tr>
<th>NH subjects</th>
<th>500-Hz threshold dB SPL</th>
<th>ERB Hz</th>
<th>EAS subjects</th>
<th>Preimplant 500-Hz threshold dB SPL</th>
<th>Preimplant ERB Hz</th>
<th>Postimplant 500-Hz threshold dB SPL</th>
<th>Postimplant ERB Hz</th>
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**Frequency Discrimination and Melody Recognition**

Finding no significant relationship among mea-
sures of auditory function and the gain in speech
understanding with EAS, we turn to melody recog-

ination to examine whether performance on mea-
sures of auditory function is related to music recog-

ination. Although an increasing number of cochlear
implant patients are able to achieve high levels of
performance on difficult measures of speech recog-

ination, most cannot recognize familiar melodies
when temporal cues are removed [31–35]. This is not surprising given the modest, at best, spectral resolution achieved with electric stimulation [36–38]. As discussed above, following successful hearing preservation surgery EAS patients have some residual frequency selectivity for low-frequency acoustic stimuli. Thus, EAS patients may be better able to resolve simple and complex pitch patterns necessary for melody recognition than patients who receive only electric stimulation.

Gfeller et al. [32] evaluated the pitch perception abilities of 101 conventional cochlear implant recipients and 13 EAS listeners with binaural acoustic hearing, i.e., patients with low-frequency hearing in both the implanted ear and in the contralateral ear. For the pitch perception task, subjects were asked to determine the direction of pitch change (i.e., higher or lower) for the second pure tone in a ‘pitch pair’. The frequency of the standard tone ranged from 131 to 1,048 Hz. The data demonstrated that the EAS subjects – implanted with a 10-mm Nucleus Hybrid device – identified the direction of pitch change, for frequencies under 663 Hz, better than conventional implant patients.

In another study, Gfeller et al. [39] evaluated melody and musical instrument recognition for 4 EAS listeners and 39 conventional implant recipients. The EAS subjects obtained significantly higher scores on tests of melody recognition and instrument recognition than the patients who received only electric stimulation.

Gfeller’s studies leave little doubt that low-frequency acoustic hearing provides information about pitch that is unavailable from electric stimulation. However, because testing was completed in the sound field using EAS patients with acoustic hearing in both the implanted ear and the nonimplanted ear, it is not clear which partially hearing ear provided the additional information. In other words, it is possible that the acoustic hearing from the implanted ear did not offer any additional benefit over the acoustic hearing provided by the nonimplanted ear.

Several studies have shown that low-frequency acoustic hearing in the ear contralateral to the implant is sufficient to significantly improve melody recognition for implant patients. For example, Dorman et al. [34] described the melody recognition abilities of 15 bimodal patients (implant in one ear and acoustic hearing in the other ear) who had relatively good residual hearing in the nonimplanted ear (e.g. thresholds at 125 and 250 Hz of 35–45 dB). The recognition of melodies without rhythmic cues was assessed for a test set of 5 familiar melodies. Recognition was significantly better in the bimodal condition than in the electric-only condition. Recognition in the bimodal condition, however, was not better than in the acoustic-only condition. Thus, we found no synergistic effect of EAS for the recognition of melodies. All of the benefit of bimodal EAS for melody recognition, relative to a conventional implant, was due to the presence of the acoustic signal. Kong et al. [35] reported similar findings for 5 bimodal subjects with much poorer residual hearing than the patients in the study by Dorman et al. [34].

One Partially Hearing Ear versus Two Partially Hearing Ears

As noted above, EAS patients will have low-frequency acoustic hearing in both the implanted ear and in the contralateral ear. The contribution of the two partially hearing ears to speech recognition is not easy to determine. Most papers have provided speech perception data for the electric-only condition, the ipsilateral EAS condition, and/or the combined EAS condition (implant plus both partially hearing ears) [2, 3, 6, 8–10]. It has not been common to report performance in the bimodal condition with the ipsilateral ear occluded. This condition is important because it is usually the case that the hearing in the contralateral ear is better than the hearing in the implanted ear, i.e., the ear with the poorer auditory thresholds is usually picked for surgery and/or the thresholds
in the operated ear are poorer following surgery than before surgery.

Dorman et al. [40] assessed the bimodal and combined EAS speech perception performance of 22 patients implanted with the 10-mm Nucleus Hybrid electrode array. They found a small, non-significant improvement of 9 percentage points in the combined condition relative to the bimodal condition. In a subset of this subject population \( n = 7 \), Gifford et al. [41] found identical scores for the bimodal and combined conditions on measures of sentence recognition in noise using the BKB-SIN test with the speech and noise originating from a single loudspeaker.

On the one hand, the data reported above cast doubt on the benefit to speech understanding of preserved hearing on the operated ear when compared to bimodal stimulation. On the other hand, the test environments in both experiments – stimulus presentation from a single loudspeaker placed at \( 0^\circ \) azimuth – minimized the value of binaural cues that could be extracted with two partially hearing ears.

When two ears, rather than one ear, are allowed to participate in a listening test, and when signal and noise are presented from different locations (as is commonly the case in the ‘real world’), then three effects – head shadow, binaural squelch and binaural (or diotic) summation – can influence performance. Head shadow is a physical effect in which the head provides an acoustic barrier resulting in amplitude or level differences between the ears. If one ear is closer to the noise source, the other ear has a higher or better signal-to-noise ratio (SNR). Binaural squelch refers to a binaural effect in which an improvement in the SNR results from a central comparison of time and intensity differences for signals and noise arriving at the two ears. Binaural summation refers to the effect of having redundant information at the two ears.

EAS patients have two acoustically stimulated ears that could code interaural time and intensity differences and two ears to deliver redundant acoustic information. From this point of view, EAS patients should have an advantage over bimodal patients when signal and noise originate from different spatial locations in a sound field. To test this hypothesis, we have collected speech perception data for conventional unilateral implant recipients \( n = 25 \), bilateral cochlear implant recipients \( n = 10 \), bimodal listeners \( n = 24 \), and EAS listeners \( n = 5 \). The 5 EAS listeners were 3 Nucleus Hybrid recipients (2 Hybrid 10 mm, 1 Hybrid-L24 16 mm) and 2 conventional Nucleus N24 (CI24RCA) long-electrode recipients with hearing preservation.

Hearing-in-noise test sentence recognition [42] was assessed in a restaurant noise background [43] originating from the R-SPACE™ 8-loudspeaker array. The 8 loudspeakers were placed circumferentially about the subject’s head at a distance of 60 cm with each speaker separated by 45°. A speech reception threshold (SRT) was obtained using an adaptive procedure to determine the SNR required for 50% correct. The noise level was fixed at 71 dB SPL to simulate the average level of the noise observed during the restaurant recording. Figure 2 displays mean SRT data for the 4 subject groups. The unilateral and bilateral implant mean data are displayed as a reference for electric-only performance.

The unilateral and bilateral mean SRT scores were 12.2 and 9.6 dB SNR, respectively. For patients with bimodal stimulation, i.e., bimodal patients and EAS patients in the bimodal condition, the SRTs were 10.6 and 9.6 dB SNR, respectively. When the EAS patients were able to access the acoustic hearing in the operated ear, performance improved by 3.4 dB to a mean SRT of 6.2 dB SNR. These preliminary data support our hypothesis that the value of hearing preservation will be best shown in listening environments in which target and masker are spatially separated and environments in which binaural low-frequency cues can play a significant role. Given that every 1-dB improvement in the SNR can translate up to 8–15% improvement in speech recognition performance [42, 44], the addition of acoustic hearing from the implanted ear has the
potential to provide large gains in speech intelligibility in complex listening environments.

Summary and Conclusions

There is ample evidence demonstrating that electrodes can be inserted into the scala tympani without destroying residual hearing and that EAS patients can combine information delivered by electric stimulation and acoustic hearing. The data presented in this paper document that it is possible to preserve normal or near-normal non-linear cochlear processing in the implanted ear following EAS surgery – though this is not the typical outcome. We have also shown that while low-frequency frequency selectivity is generally disrupted following implantation, some degree of frequency selectivity can be preserved. And, in a surprising outcome, we find that neither non-linear cochlear processing nor frequency selectivity in the acoustically stimulated ear is correlated with the gain in speech understanding when acoustic stimulation is added to electric stimulation.

The goal of hearing preservation surgery is to preserve hearing in the implanted ear. However, to date, it has not been clear whether significant benefit is gained from having two acoustic hearing ears (as in the case of EAS) versus just one (as in the case of bimodal stimulation). Our results demonstrate the benefit of hearing preservation in the implanted ear, i.e., having two acoustic hearing ears, for speech perception in a complex listening environment. Given the preliminary nature of the data, further study is warranted to fully describe the benefits of preserving acoustic hearing following cochlear implantation.

Acknowledgements

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References


Neuronal Responses in Cat Inferior Colliculus to Combined Acoustic and Electric Stimulation

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Abstract
The present study explored the interactions of combined electric and acoustic stimulation (EAS) on neural responses in the central auditory system. Normal-hearing cats were implanted unilaterally with scala tympani electrodes. Two experimental approaches were used. First, in a forward-masking paradigm, single biphasic electric pulses were used as maskers, unmodulated acoustic tone bursts at the neuron's characteristic frequency (CF) were used as probes. Then, in a simultaneous-masking paradigm, the masking effects of acoustic tones (CF) on responses to single electric pulses (probes) were examined. In the second approach, we studied the effects of phase relationship between acoustic and electric stimulation. Sinusoidal amplitude-modulated (30 Hz) CF tones and electric sinusoids (30 Hz) were shifted in relative phase (0–270°). For all experimental conditions, the levels of the two stimuli were changed systematically. Responses were recorded in the contralateral central nucleus of the inferior colliculus. Single neuron analyses of spike rate and thresholds demonstrated that combined EAS resulted in complex interactions that were strongly dependent on the relative level of the given stimulus modes. The amount of masking increased with masker level and decreased with probe level. At higher current levels, the masking effect of electric responses dominated the effect of acoustic responses. The degree of these general masking effects was highly influenced by the relative phase between the combined stimuli. It seems likely that such interactions of combined stimulation have perceptual consequences in human cochlear implant subjects with residual hearing.

Due to synergistic effects combined acoustic and electric stimulation (EAS) of the auditory system provides significant benefits in speech perception – especially in noisy environments – to a high proportion of cochlear implant (CI) subjects with preserved low-frequency hearing when compared to acoustic or electric stimulation alone [1–5]. The mechanisms underlying such improvements and the encoding of combined EAS at any level of the auditory system are largely unknown. Aside from beneficial interactions between acoustic and electric stimulation, there also remains the possibility of disturbing interferences. Physiological studies of neuronal responses are required to better understand and take advantage of the functional interactions between acoustic and electric stimulation.

Using simultaneous- and forward-masking paradigms previous studies on the interactions of combined EAS have mainly focused on responses from the auditory nerve and examined the effects of broadband acoustic noise on electrically evoked compound action potentials (ECAPs) [6, 7] and single auditory nerve fiber (ANF) responses [2, 8–10]. Acoustic masking of electrically evoked responses was observed for both ECAP (decreased amplitudes) and single ANF measures (increased...
ANF thresholds, reduced firing synchrony). These effects were attributed to a desynchronizing simultaneous effect of acoustic stimulation on ANF responses and reduced ANF responses after the cessation of the acoustic stimulus due to continuing suppression of ANF spontaneous activity [11, 12]. Combined spike rate of single ANFs almost always increased during combined EAS. In addition, ANF spike rates and temporal firing patterns to combined EAS were strongly dependent upon the relative levels of both the acoustic and electric stimulus. At high electric levels, electric stimulation dominated the combined response to EAS.

The goal of the present study was to describe interactions of EAS in the central auditory system at the level of the central nucleus of the inferior colliculus (ICC). In a first experimental approach, we used a forward-masking paradigm to study the effects of electric stimuli on acoustically evoked response rates and thresholds. Using the same experimental setup, we then studied the simultaneous effects of acoustic stimulation on electrically evoked responses. For acoustic stimulation, tone bursts at the neuron’s characteristic frequency (CF) were used. For electric stimulation, single electric pulses were presented at very low rates (33.33 pulses/s) to avoid adaptation effects.

Because sinusoidal amplitude-modulated (SAM) signals are used in contemporary speech processing strategies, possible effects of phase relationships between combined acoustic and electric stimulation are likely to affect speech perception in CI users with residual hearing. In a second experimental approach, we, therefore, studied phase effects of combined responses by shifting the relative phase between simultaneously presented SAM (30 Hz) CF tones and electric sine waves (30 Hz) by 0, 90, 180 and 270°. In order to explore the level dependence of acoustic-electric interactions, the levels of the acoustic and the electric stimuli were varied systematically in all experimental approaches. Responses were recorded for acoustic-only stimulation, electric-only stimulation and combined stimulation (EAS) to assess the acoustic and electric interactions against baseline measures.

**Methods**

**Surgery**

All the experiments were approved by the local state authority and were performed in compliance with the guidelines of the European Community for the Care and Use of Laboratory Animals (EU VD 86/609/EEC). Experiments were performed in adult normal-hearing cats. Animals were sedated with ketamine hydrochloride (24.5 mg/kg) and propionyl promazine phosphate (2.1 mg/kg). Atropine (0.5 mg i.p.) was applied at the beginning of the experiment to reduce salivation. Anesthesia was maintained by additional doses of pentobarbital (32 mg/kg). The trachea was cannulated, and the animals were artificially ventilated. End-tidal CO2, heart rate and body temperature were monitored regularly [13]. After removing the external meatus to allow the use of a controlled closed sound delivery system one bulla was exposed, and the round window (RW) was opened. A custom-made feline electrode array consisting of a silicone carrier with 4 platinum-iridium contacts (diameter approx. 380 μm, spacing 2 mm; MED-EL) was inserted through the RW. The apical-most electrode contact was located at around the 9-kHz region along the basilar membrane. Acoustic sensitivity was repeatedly assessed during the experiments by measuring acoustically evoked compound action potentials (ACAPs) with a silver wire positioned in the RW niche.

The inferior colliculus contralateral to the implanted cochlea was exposed [14]. Neuronal responses were recorded using parylene-coated tungsten microelectrodes (impedances of 0.8–1.5 MΩ at 1 kHz) mounted on a 3-dimensional micromanipulator (ORIEL resolution 1 μm). Electrode penetrations were orientated at an angle of 45° from the vertical plane parallel to the tonotopic gradient with low frequencies presented at the dorsolateral and high frequencies at the ventromedial aspect of the inferior colliculus.

**Acoustic Stimulation**

Experiments were performed in an electrically shielded sound-attenuating chamber. Acoustic stimuli were generated using a multifunction I/O board (National Instrument, MIO-16E-1) housed in a PC and custom-made software. Stimuli were delivered by an inversely driven condenser microphone (1-inch B+K 4145) close to the eardrum.

Acoustic clicks (condensation and rarefaction, 50 μs duration, 8.8 Hz) were used for ACAP threshold measures to monitor hearing sensitivity. To measure ICC frequency response areas and to determine the CF of the neurons,
gated tones of 30 ms duration (5-ms leading and trailing slopes) were presented at frequencies ranging from 100 Hz to 40 kHz in 1/3 octave steps. Sound pressure levels were monitored by a Sennheiser KE4 microphone. The acoustic stimuli were attenuated by a custom-made attenuator (0 dB attenuation = 124 dB SPL, 1-dB steps).

For the forward- and simultaneous-masking paradigms in the first experimental approach, single 50-ms unmodulated tone bursts (including a 5-ms cosine on/off ramp) were presented at the neuron’s CF (schematic in fig. 1a). To measure phase effects, 4 cycles of SAM tones (100% modulation depth) were used. The carrier was presented at the neuron’s CF, the modulation frequency was 30 Hz. The intertrial intervals were usually 1,000 ms to prevent neural adaptation.

Electric Stimulation

Electric stimuli consisted of 3 single charge-balanced biphasic pulses (200 μs/phase) presented at a low rate (33.33 pulses/s; fig. 1a) or 4 cycles of a 30-Hz sinusoid (Rockland sine wave generator 5100; fig. 2a, b). Stimuli were applied in a bipolar mode using the 2 most apical electrode contacts. Electric stimuli were computer controlled and delivered to the electrode contacts by an optically isolated constant current source (MED-EL type IS 2).

Recording

For ACAP recordings the responses were amplified by 60–80 dB (Tektronix type 122,5A22N), band-pass filtered (0.1–3 kHz), sampled with a rate of 25 kHz by an A/D card (PCI-MIO-16E-1, National Instruments) and stored for off-line analysis. The same setup was used to record from single-units and multiunits, but responses were amplified by 100–106 dB and band-pass filtered between 1 and 3 kHz.

Experimental Procedure

Initially, the acoustic response areas and the CFs of ICC neurons were determined. In the first experimental approach, acoustic-only thresholds to 50-ms tone bursts at CF and electric-only thresholds to biphasic pulses (33.33 pulses/s, 3 pulses) were determined. Subsequently, acoustic tone bursts at CF and electric pulse trains were presented simultaneously. Figure 1a demonstrates a schematic of the combined stimulation. For a set of fixed electric currents (subthreshold, 1–8 dB re threshold in 1-dB steps) the acoustic levels were varied between subthreshold and 20 dB re threshold (5-dB steps). Because the first electric pulse occurred at the beginning of the acoustic on-ramp and because acoustic responses have typically longer response latencies than electric responses (e.g. due to the traveling wave along the basilar membrane) the influence of the first pulse on the acoustic onset response is regarded as a forward-masking effect whereas acoustic effects on the second pulse represent a simultaneous-masking condition.

In the second experimental approach, neuronal thresholds to 4 cycles of SAM tone bursts (carrier at CF, envelope 30 Hz) and 4 cycles of electric sinusoids (30 Hz) were determined separately. To investigate the effects of phase shifts, these SAM tone bursts and cycles of electrical sinusoids were then presented simultaneously. Acoustic and electric stimulus levels were varied systematically. Stimuli always started at zero amplitude. The electric stimulus was delivered at different phases relative to the envelope of the acoustic stimulus (0, 90, 180 and 270°). Acoustic as well as cochlear delays (traveling wave, filter delays) were not taken into account. For each stimulus condition responses to at least 20 repetitions were recorded. Throughout the article, all acoustic and electric levels will be reported relative to acoustic-only and electric-only thresholds, respectively (threshold = 0 dB).

Data Analysis

Data were analyzed off-line using spike2 software (v4.03 Cambridge electronic design) for spike sorting. Matlab and Excel were used for subsequent quantitative analyses of single-unit responses.

Results

Forward and Simultaneous Masking

Figures 1a–c demonstrate examples of multineuronal responses to combined EAS for varying acoustic and fixed electric stimulus levels. For the acoustic stimulus component a 50-ms tone burst at the neuron’s CF was used; the electric stimulus component consisted of 3 single biphasic pulses (0.2 ms/phase) presented at 33.33 pulses/s. In figure 1a, the electric stimulus is presented at subthreshold level. Thus, this figure only displays the (predominant onset) responses to the acoustic stimulus alone. The horizontal dashed line indicates the acoustic threshold for acoustic-only stimulation and is repeated in figures 1b and c. Figures 1b and c demonstrate the increases in acoustic thresholds in the presence of increasing electric stimulus levels when compared to acoustic-only stimulation.

Figure 1b displays the two time windows used for analysis. Comparisons of spike rates in window 1 reflect the forward-masking effects of the responses to the first electric pulse on the acoustic onset responses. Spike rates in window 2
**Fig. 1.** a–c Raster histograms of multineuronal responses to combined EAS. Increasing acoustic levels (normalized to acoustic-only threshold) are noted on the ordinate. Electric levels (normalized to electric-only threshold) are noted in the upper right of each histogram. Relative timing of the acoustic tone (presented at the fiber’s CF) and the electric pulses (3 biphasic pulses at 33.33 pulses/s) is shown schematically in a. Squares in b indicate time windows used for analysis of neuronal responses. The dashed line means acoustic-only threshold, repeated in a–c. d Mean normalized acoustic spike count derived from analysis window 1 (b) as a function of normalized electric level. Parameter is normalized acoustic level. n = Number of single neurons. For clarity, error bars were not included. e Mean acoustic threshold shifts (analysis window 1) for increasing electric levels (normalized). Bars indicate standard deviation. f Mean normalized electric spike count from analysis window 2 (b) plotted for increasing normalized acoustic levels. Parameter is normalized electric level. Bars: standard error. Inset displays slopes of linear regressions for each of the functions.
demonstrate the simultaneous-masking effects of the acoustic (onset) responses on the responses to the second electric pulse.

Figures 1d–f summarizes the spike rate and threshold results for 6 single neurons for which complete recording series for all given level combinations could be obtained. The data in figures 1d and e are derived from window 1 and demonstrate the effect of a single electric pulse on acoustic responses. Figure 1d shows the normalized acoustic spike rates for increasing electric levels. The parameter is acoustic level. As expected, the overall spike rate increased with increasing acoustic level. However, the presence of a preceding electric masker pulse suppressed the acoustic responses. This masking effect increased with increasing electric level and resulted in elevated acoustic response thresholds. Figure 1e summarizes the acoustic threshold shifts for increasing electric forward masker levels. For increases in electric level to 7 dB re electric-only threshold, an acoustic threshold shift of 11 dB was observed.

Figure 1f shows the normalized single neuron spike rates as a function of acoustic stimulus level for window 2 and, thus, demonstrates the effect of acoustic responses on the responses to a single electric pulse. The parameter is electric level. Similar to the acoustic responses, overall electric spike rates increased with increasing stimulus level. The simultaneous presentation of acoustic tone stimulation led to a suppression of the electric spike rate. The degree of masking of electric responses increased with increasing acoustic level. The inset in figure 1f shows the slopes of linear regressions fitted to each of the functions. For threshold and suprathreshold electric stimulus levels, all slopes were negative, reflecting the masking effect by the simultaneous acoustic responses. The slopes were the steepest around 1 dB above the electric-only threshold and became shallower with increasing electric levels. These results suggest that relatively low suprathreshold electric stimulus levels can largely overcome the acoustic masking effect. This strong electric countereffect on acoustic masking may, of course, be well related to the overall small dynamic range of electric stimulation [15] and the limited range of acoustic suprathreshold masker levels used in the present study (up to +20 dB). The overall electric threshold shift in the presence of an acoustic masker presented at +20 dB re acoustic-only threshold was only 1 dB (not shown).

Phase Shifts

The effects of relative phase shifts between acoustic and electric stimuli of varying levels on neuronal responses are illustrated in figure 2. Acoustic SAM (30 Hz) tones at CF and electric sinusoids (30 Hz) were simultaneously presented starting at zero amplitude, and the electric stimulus was delivered at different phases (0, 90, 180 and 270°) relative to the envelope of the acoustic stimulus. It is important to note that the relative phase does not refer to the phase relationship along the basilar membrane, as we do not account for any cochlear delays. Because of differences in cochlear delays (e.g. due to different CFs), the resulting EAS interactions for a given phase relationship varied across neurons. It was, therefore, problematic to pool data from different neurons. The examples of responses shown in figure 2 are derived from a single neuron. However, the phenomena associated with these examples appear in other neurons that show overall similar response patterns to phase shifts in combined EAS.

Figures 2a and b show exemplary raster histograms of responses from one neuronal cluster to relative phase shifts of 90 and 270°. In these examples, acoustic levels are increasing along the ordinate, and electric stimulation is presented at a fixed level (+4 dB re electric-only threshold). Acoustic level-dependent differences in the response strength (spike rate) and temporal precision (jitter and phase locking) for different phase relations of combined EAS are apparent in figures 2a and b. At 90°, the electric and acoustic
Fig. 2. a, b Examples of raster histograms of multineuronal responses to combined EAS. Increasing acoustic levels are noted on the ordinate. Electric levels and relative phase shifts are noted in the upper right of each histogram. Relative timing and phase shifts of the acoustic stimulus (carrier at CF, SAM 30 Hz) and the electric sinusoid (30 Hz) are shown schematically. c–f Spike counts of a single neuron plotted as a function of acoustic level for relative phase shifts of 0–270° (noted in the upper left corner of each graph). Parameter is electric level. Dashed function indicates spike count for acoustic-only stimulation.
responses nearly completely overlapped, whereas at 270° the two responses are interleaved and display mutual suppression.

Because responses to the acoustic and electric stimulus components often could not be separated, combined spikes for each level combination were counted over the entire stimulus window (200 ms) to quantify the overall effects of phase interactions. To allow within-neuron comparisons spike counts of a single neuron were plotted as a function of the acoustic level for the 4 different phase shifts (fig. 2c–f). The parameter was the level of the simultaneously presented electric stimulus. The dashed line indicates spike count to acoustic-only stimulation and is repeated in each graph.

For any given suprathreshold level combination between acoustic and electric stimulation, the response rates were highly dependent on the relative phase between the two modes of stimulation. With the exception of responses to higher electric current levels for 0° phase shift and to 4 dB for 270°, nearly all suprathreshold level combinations of acoustic and electric stimulation generally resulted in an increase in combined spike rate (EA) when compared to the spike rate to electric-only (E) stimulation (i.e., EA/E ratio >1). However, the spike rate to combined EAS could not simply be predicted by the addition of acoustic-only and electric-only responses. Instead, in almost all cases the measured spike rates to combined stimulation were lower than those predicted by linear summation of each same-level stimulus condition alone. This difference between the measured and predicted spike rate values generally increased with higher electric current levels and was particularly large for responses to 0° phase shift. Moreover, the ratio of spike rate between combined EAS and electric-only stimulation (EA/E ratio) was generally largest at low suprathreshold electric levels but decreased at higher electric levels, suggesting a greater influence of the electric stimulation on combined spike rate at higher current levels. Although the described effects of electric current level on responses to combined stimulation held generally true for all conditions tested, the overall magnitude of EA/E ratios covered a large range (0.9–14.4) and strongly varied with the relative phase between the combined stimuli. Within the limited range of acoustic levels tested, acoustic stimulation had only little effect on EA/E spike rate ratios. However, with the exception of responses to higher electric current levels at 0° phase shifts, EA/E spike rate ratios rarely reached the asymptotic value of 1 or below even at the highest electric levels used in the present study, indicating that electric stimulation usually did not fully mask the acoustic responses during combined stimulation.

Conclusions

The results of the present study demonstrate complex functional interactions between acoustic and electric cochlear stimulation at the level of the ICC in hearing subjects. These mutual interactions were highly dependent on the relative level and phase between the two signals.

Forward and Simultaneous Masking with Unmodulated Stimuli

The separate analysis of the data by acoustically and electrically evoked spike rates (fig. 1) allowed us to assess the relative impact of changes in acoustic and electric stimulus levels. Both forward masking (effect of electric on following acoustic responses) and simultaneous masking (effect of acoustic stimulation on simultaneous electric responses) resulted in decreased firing rates and increased thresholds of the probe responses. These effects were highly level dependent and were more pronounced at higher masker and lower probe levels.

These findings are in agreement with earlier studies of simultaneous and forward (or post-stimulatory) masking effects at the level of the auditory nerve [10, 12, 16–18]. These studies reported changes in both gross potential (ECAP) amplitudes and single ANF firing rates in response to electric probe pulses that were strongly
dependent on the level of the acoustic noise masker. Specifically, they described larger reductions and slower recovery in ECAP amplitudes and increases in single ANF thresholds and reduced firing synchrony.

The masking effects of acoustic and electric stimuli can differ fundamentally. The strong influence of electric stimulus level on acoustic thresholds (fig. 1e) and the finding that acoustic suppression of electric responses is greatest for a narrow range of electric levels around electric-only thresholds with decreasing masking effects at higher electric levels (fig. 1f) suggest that at moderate to high electric current levels the relative influence of electric masking in combined EAS dominates that of acoustic stimulation. This is consistent with the higher synchrony of electric responses when compared to acoustic responses, the relatively small dynamic range especially for pulsatile electric stimulation that results in widespread activation patterns at relatively low suprathreshold levels [15] and the finding that electric stimulation can lead to higher ANF discharge rates than acoustic stimulation [19]. However, results in the present study are limited to stimulation with acoustic levels of maximally 20 dB re acoustic-only threshold. Further measures with acoustic levels that cover a larger part of the dynamic range of acoustic hearing are required to more reliably estimate the relative influence of one kind of stimulus against the other.

**Effects of Relative Phase**

The effects of relative phase were examined on the basis of within-neuron comparisons of combined spike rates evoked by the simultaneous presentation of acoustic SAM signals and electric sinusoids of varying levels. At suprathreshold levels, combined stimulation resulted in increased spike rates in most conditions. However, the combined spike rate typically did not increase linearly and was highly dependent on the relative phase between the acoustic and electric stimulation. Within a given phase relationship electric stimulation dominated the combined responses, especially at higher current levels. This is again consistent with the above-mentioned lower dynamic ranges [15] and greater spike rate in response to electric pulses [19] when compared to acoustic stimulation. The reported results have to be tested also for larger ranges of acoustic levels.

The present findings are in close agreement with across-fiber ANF responses to simultaneous stimulation using unmodulated electric pulse trains and acoustic noise [10]. Although Miller and colleagues [10] used across-fiber comparisons and did not examine the effects of relative phase shifts between combined stimulation, they confirmed the relative dominance of electric stimulation at higher levels and observed increases in spike rates for most conditions of combined stimulation that fell short of a simple linear summation.

**Clinical Implications**

The relaxation of audiologic criteria for cochlear implantation of subjects with wider ranges of residual hearing and the trend towards greater insertion depths of the electrode array will minimize the functional gap between the acoustically sensitive and the electrically driven frequency regions along the cochlea. In addition, animal studies in the ICC have shown that pulsatile electric stimulation has a very narrow dynamic range that can lead to unselective activation of large neuronal populations at relatively low suprathreshold current levels [15]. As a result, a spatial overlap of combined EAS within populations of peripheral and central auditory neurons is highly likely, and complex interactions, as described in the present study, may well influence the overall effectiveness of combined EAS in human CI subjects with residual hearing. For the design of future EAS speech processing strategies, further single and multineuronal studies are required to establish a better understanding and to, consequently, take advantage of both the spatial activation patterns and the temporal interactions of combined EAS in the peripheral and central auditory system.
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Music Perception in Electric Acoustic Stimulation Users as Assessed by the Mu.S.I.C. Test

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Abstract

Aims: This study compared the music perception abilities of 13 electric acoustic stimulation (EAS) users with two control groups: unilateral cochlear implant (CI) users and normal-hearing (NH) listeners. Methods: Groups were matched according to age and musical experience before hearing loss (HL) and tested using the Musical Sounds in Cochlear Implants (Mu.S.I.C.) test. Results: No difference was found on rhythm perception, chord discrimination, dissonance rating, and emotion rating subtest performance between groups. Mean frequency discrimination scores were significantly better in EAS participants than in CI participants and not significantly worse than in NH participants. However, the EAS and CI groups scored similarly (significantly worse than NH participants) on both instrument detection and identification. Results for EAS participants were not significantly worse when the hearing aid component was removed. Frequency of listening to music before HL was negatively correlated with EAS participants’ frequency discrimination scores, though singing and playing an instrument appeared to have no effect. EAS participants who indicated many reasons for listening to music and who listen to many genres after implantation scored higher on instrument detection and instrument identification. Better results on these two subtests were correlated with EAS participants’ better postoperative auditory thresholds at 250 and 500 Hz. Conclusions: Though EAS participants performed better on music perception testing (though not timbre-based tasks) than CI participants, their scores did not reach the level of NH participants. This indicates that acoustic hearing in the low frequencies is helpful for music perception, though not the only important factor.

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Several hundred people worldwide with residual hearing in the low frequencies are currently using combined electric and acoustic stimulation (EAS) devices, and it is estimated that many more could benefit from this technique. Since the first EAS surgery in Frankfurt in 1999, the ability to preserve low-frequency residual hearing in the majority of cases [1–3] and the improved speech perception outcomes [2–4] have been widely documented. However, there are currently very little published data on EAS users’ ability to perceive and enjoy music.

The existing literature on unilateral cochlear implant (CI) users’ abilities shows that performance
varies greatly depending on the aspects of musical abilities tested [5]. This may be different for bilateral CI users, though, as recent findings indicate that approximately 95.5% of bilateral CI users compared with 66% of unilateral CI users listen to music regularly [6, 7] and that most aspects of music perception are enhanced by bilateral implantation [8].

In the only published study on music perception in EAS users, Gfeller et al. [9] tested a group of 4 Nucleus Hybrid CI users and found that they performed significantly better than CI users on melody recognition with lyrics. Fourteen Hybrid users in the same study performed significantly better than CI users on low- and high-frequency instrument recognition.

This investigation aimed to gain insight into the music perception abilities of EAS users by comparing their performance on objective and subjective measures with that of unilateral CI users and normal-hearing (NH) listeners. This was done using the Musical Sounds in Cochlear Implants (Mu.S.I.C.) test [10], a custom-designed assessment of various aspects of music listening abilities, and the Munich Music Questionnaire (MUMU) [11].

Methods

Participants

EAS Users. All 13 participants met inclusion criteria for EAS candidacy as described by Kiefer et al. [4]. Mean age at implantation of the EAS group was 53 years (range = 25–65). All EAS participants underwent EAS surgery as described by Kiefer et al. [4] and received a MED-EL COMBI 40+ CI with a standard electrode and CIS+ speech coding strategy. Consistent with Kiefer et al. [1], after a period of 3 months using the CI only, EAS participants were fitted with a Resound® hearing aid (HA) in the same ear. For participants in the study, fitting parameters had to be stable and participants were required to have 6 or more months of EAS use. Mean EAS experience for the group was 2.1 years (range = 0.5–3.3). EAS patients were tested in two conditions: CI + HA (EAS mode) and CI-only (HA deactivated). The frequency range transmitted by the speech processor was identical in both conditions. Two of the 13 EAS participants did not use HAs on the contralateral ear. For testing CI-only, the contralateral ear was blocked with an 8-dB earplug. Three patients were excluded from CI-only analyses because we assumed that their residual hearing in the low frequencies could not be attenuated sufficiently.

Controls – NH and Unilaterally Implanted CI Participants. The CI participants were chosen from a database of COMBI 40+ and NH participants from an ongoing study. NH was defined according to Jatho and Heck [12]. All CI participants were postlingually deaf with a minimum implant experience of 6 months (range = 0.5–5.2 years; mean = 2.8 years)

Matching Criteria. The EAS and CI participants were matched for age and musical experience before hearing loss (HL). Musical experience was assessed using the responses to 3 MUMU questions (table 1) [6]. The criteria for matching the NH participants were age and present musical activities. Professional musicians were excluded from the study. No group differences were significant: listening to music (EAS/NH: p = 0.588; EAS/CI: p = 0.566), playing an instrument (EAS/NH: p = 0.988; EAS/CI: p = 0.704), singing (EAS/NH: p = 0.544; EAS/CI: p = 0.301), MUMU total score (EAS/NH: p = 0.769; EAS/CI: p = 0.436), and age at testing (EAS/NH: p = 0.471; EAS/CI: p = 0.99).

The Mu.S.I.C. Test

The Mu.S.I.C. test [9] battery consists of 6 objective subtests assessing aspects of pitch, rhythm, melody, harmony and timbre perception and 2 subjective subtests assessing emotion and dissonance perception. More detailed information on technical aspects and administration for each subtest can be found in the Mu.S.I.C. test user guide (available online: http://www.medel.at/english/50_Rehabilitation/Free-download/index.php?navid=40&r=1&r=1&r=1), except for melody discrimination because it has been altered since this study. The battery contains approximately 2,800 sound files recorded at the Royal Scottish Academy of Music and Drama by professional musicians playing natural instruments. Participants’ Mu.S.I.C. test scores were stored in an MS Access database with encrypted personal data.

Test Procedure. Participants sat in a quiet room and wore Sennheiser HD 570 headphones to make the testing condition more standard across centers. At the beginning of each subtest, participants were asked to adjust loudness to a comfortable level. Written instructions for each task were given to every participant in their respective native language with the audiologist available throughout testing to give further explanation, if requested. Before each subtest (except instrument identification), two demonstrations were given. Participants were informed that they could take breaks during and between subtests. One repetition per item was allowed
except on pitch discrimination because pitch ranking procedures do not allow this. For testing in the CI-only condition, the unimplanted ears of CI and EAS participants with residual hearing were plugged as were the ipsilateral ears of EAS participants during testing in the CI-only condition.

**Test Configuration.** In this feasibility study, a representative subset of the sound files available in the Mu.S.I.C. test was used. For the pitch ranking in pitch discrimination, 3 staircases were interwoven. We used: piano with a target note of C4 (262 Hz), strings with a target note of A4 (440 Hz) and pure tones with a target note of F4 (349 Hz). For melody discrimination, 18 samples were chosen from each of the 7 levels available. Five pairs from each of the 3 levels of difficulty were chosen for rhythm discrimination and 4 were chosen from the 3 levels for chord discrimination. Instrument detection included these combinations: (1 instrument) cello; (2 instruments) cello and xylophone; (3 instruments) double bass, flute, and trumpet; (4 instruments) cello, double bass, flute, and xylophone; (5 instruments) flute, double bass, cello, trumpet, and xylophone. Each permutation was presented once. Instrument identification featured double bass, flute, bassoon, piano, xylophone and soprano singer. Each of the instruments was presented with a characteristic piece, ‘Baa Baa Black Sheep’ and a scale at a typical range for the instrument. There were 5 more instrument icons displayed than instruments recorded, so that there was a distracter for each instrument (e.g. violin for double bass). Emotion rating was tested with all 32 samples and dissonance rating, with 4 files for each of the 3 levels of dissonance.

<table>
<thead>
<tr>
<th>Participant ID</th>
<th>Listening</th>
<th>Playing an instrument</th>
<th>Singing</th>
<th>Total score</th>
<th>Age at testing, years</th>
</tr>
</thead>
<tbody>
<tr>
<td>NH1</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>11</td>
<td>55</td>
</tr>
<tr>
<td>NH2</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>12</td>
<td>48</td>
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<td>14</td>
<td>66</td>
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<td>9</td>
<td>56</td>
</tr>
<tr>
<td>NH6</td>
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<td>5</td>
<td>1</td>
<td>10</td>
<td>64</td>
</tr>
<tr>
<td>NH7</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>11</td>
<td>36</td>
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<tr>
<td>NH8</td>
<td>3</td>
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<td>3</td>
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<tr>
<td>NH9</td>
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<td>51</td>
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<tr>
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<td>5</td>
<td>5</td>
<td>15</td>
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<tr>
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<td>4</td>
<td>3</td>
<td>3</td>
<td>10</td>
<td>53.0</td>
</tr>
</tbody>
</table>

Values for these questions are based on a Likert scale: 1 = Never; 2 = seldom; 3 = average; 4 = often; 5 = very often. Total score is the sum of listening, playing an instrument and singing.
Munich Music Questionnaire
The MUMU [6, 10] was used to assess participants’ subjective impressions of listening to music, previous musical experience, and present musical activities. The version of the MUMU used in this study was adapted for unilateral CI and NH participants. It contains 18 questions on listening to music, playing music, and singing before onset of HL (EAS and CI participants), after implantation (EAS and CI participants) and at the present time (NH participants). A current version of the MUMU [11] is downloadable at www.medel.com.

Data Analyses
Participants were matched according to chronological age and indicators of previous musical experience (table 1).

<table>
<thead>
<tr>
<th>Singing Total</th>
<th>Score</th>
<th>Age at testing, years</th>
<th>Participant ID</th>
<th>Listening</th>
<th>Playing an instrument</th>
<th>Singing</th>
<th>Total score</th>
<th>Age at testing, years</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>11</td>
<td>46</td>
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<td>61</td>
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<td>6</td>
<td>45</td>
<td>CI9</td>
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<td>1</td>
<td>1</td>
<td>6</td>
<td>38</td>
</tr>
<tr>
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<td>14</td>
<td>31</td>
<td>CI10</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>8</td>
<td>27</td>
</tr>
<tr>
<td>4</td>
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<td>CI11</td>
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<td>7</td>
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<td>CI13</td>
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<td>3</td>
<td>8</td>
<td>55</td>
</tr>
<tr>
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<td>11</td>
<td>48.6</td>
<td>CI14</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>10</td>
<td>48.1</td>
</tr>
</tbody>
</table>
paired comparison with the Mann-Whitney U test was applied to compare these two groups.

The same procedure was applied to test EAS patients in the EAS and CI-only conditions; for within-group comparisons, the Wilcoxon signed-rank test and the Friedman test were used.

Correlations between Mu.S.I.C test and MUMU results were evaluated using Spearman's correlation coefficient.

## Results

Group results on all Mu.S.I.C. subtests are found in table 2. EAS participants' Mu.S.I.C. test performance in the CI-only condition was poorer for all subtests (table 2) than their performance in the EAS condition, though not significantly (p > 0.05, for all).

### Table 2. Comparison of Mu.S.I.C. test results between EAS, CI, and NH groups

<table>
<thead>
<tr>
<th>Mu.S.I.C. subtests</th>
<th>Measure</th>
<th>NH</th>
<th>CI</th>
<th>EAS users – EAS condition</th>
<th>EAS users – CI-only condition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pitch discrimination</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piano</td>
<td>quarter tones</td>
<td>2.0 (1.5)</td>
<td>20.1 (8.9)**</td>
<td>4.2 (6.9)</td>
<td>6.5 (10.5)</td>
</tr>
<tr>
<td>Strings</td>
<td>quarter tones</td>
<td>2.1 (2.2)</td>
<td>14.7 (10.8)</td>
<td>6.6 (8.7)</td>
<td>6.6 (4.8)</td>
</tr>
<tr>
<td>Pure tones</td>
<td>quarter tones</td>
<td>1.8 (2.1)</td>
<td>12.7 (8.8)**</td>
<td>4.6 (7.0)</td>
<td>7.3 (9.0)</td>
</tr>
<tr>
<td>Melody discrimination</td>
<td>category</td>
<td>6.8 (0.4)</td>
<td>3.8 (2.8)</td>
<td>5.6 (1.9)</td>
<td>5.0 (2.0)</td>
</tr>
<tr>
<td>Chord discrimination</td>
<td>% correct</td>
<td>83.3 (13.6)</td>
<td>78.9 (13.4)*</td>
<td>87.8 (11.6)</td>
<td>78.3 (16.3)</td>
</tr>
<tr>
<td>Rhythm discrimination</td>
<td>% correct</td>
<td>82.1 (11.6)</td>
<td>77.4 (17.1)</td>
<td>84.1 (11.1)</td>
<td>79.3 (15.3)</td>
</tr>
<tr>
<td>Instrument detection</td>
<td>% correct</td>
<td>70.8 (24.0)**</td>
<td>35.4 (20.3)</td>
<td>33.8 (23.6)</td>
<td>48.0 (25.3)</td>
</tr>
<tr>
<td>Instrument identification</td>
<td>% correct</td>
<td>79.1 (18.3)*</td>
<td>52.6 (12.3)</td>
<td>60.3 (18.3)</td>
<td>47.8 (10.9)</td>
</tr>
<tr>
<td>Dissonance rating</td>
<td>visual analogue scale</td>
<td>5.2 (2.5)</td>
<td>5.2 (2.3)*</td>
<td>5.0 (1.9)</td>
<td>5.1 (1.0)</td>
</tr>
<tr>
<td>Emotion rating</td>
<td>visual analogue scale</td>
<td>4.9 (2.1)</td>
<td>5.4 (2.5)**</td>
<td>4.8 (2.4)</td>
<td>4.7 (2.4)</td>
</tr>
</tbody>
</table>

Significant differences between EAS participants in the EAS condition and the NH and CI groups are shown as:

** p < 0.001; * p < 0.05. Standard deviations are given in parentheses.

**Comparison of Electric Acoustic Stimulation, Cochlear Implant, and Normal-Hearing Groups by Mu.S.I.C. Subtests**

**Pitch Discrimination.** The EAS participants performed better than CI participants on pitch discrimination for all instruments. For the piano, pure tone and the mean value of the 3 instruments, this difference was statistically significant (piano: p = 0.001; pure tone: p = 0.003; mean of the 3: p = 0.001). The results for the violin also showed a tendency towards significance (p = 0.062). Compared with NH participants, the EAS group's frequency discrimination was worse for all instruments, though not significantly (p = 0.180, for each; p = 0.063, for mean of all 3). For the NH and EAS participants, the results of the Friedman test did not show significant differences between
Music Perception in EAS Users as Assessed by the Mu.S.I.C. Test

the instruments (EAS: $p = 0.206$; NH: $p = 0.548$). For the CI group, the difference between instruments was significant ($p = 0.017$); the results for the piano were significantly worse than for the violin ($p = 0.045$) and pure tone ($p = 0.061$).

Melody Discrimination. The EAS participants performed better on melody discrimination than CI participants, though not significantly ($p = 0.109$). Compared with NH participants EAS participants’ results were significantly worse ($p = 0.003$).

Chord Discrimination. No significant difference was found in the three groups’ performance on chord discrimination ($p = 0.150$).

Rhythm Discrimination. There was no significant difference in performance on rhythm discrimination between the three groups ($p = 0.312$).

Instrument Detection. Both EAS and CI participants performed significantly poorer on instrument detection than NH participants ($p < 0.001$, for all) (fig. 1). There was no difference in performance between the EAS and CI groups ($p = 0.876$).

Instrument Identification. The EAS participants performed better on instrument identification than CI participants, though not significantly ($p = 0.252$). EAS participants’ performance on instrument identification was significantly worse ($p = 0.021$) than NH participants’. NH participants achieved better results for individual instruments than the other two groups (fig. 2). The difference between the NH versus CI and EAS groups was statistically significant for flute ($p < 0.02$, for both). EAS participants were better than CI participants at identifying most instruments (except bassoon and piano). The differences in performance between the EAS and NH groups were statistically significant for flute only ($p = 0.005$). Error patterns across all three groups were similar. Confusions happened either within one instrument family or within a frequency range.

Dissonance Rating. Analysis of average ratings for all chords showed no significant differences between the groups ($p > 0.50$).

Emotion Rating. EAS and NH participants rated the pieces similarly, but the CI participants tended towards happier assessments, though the difference was not significant ($p = 0.538$).

Correlations of Electric Acoustic Stimulation Participants’ Mu.S.I.C. Test Results in the Electric Acoustic Stimulation Condition

EAS participants’ results on frequency discrimination for the piano, violin and pure tones were highly significantly correlated (for all: $r > 0.85$, $p < 0.001$). The mean value for the 3 instruments correlated significantly positively with performance on chord discrimination ($r = 0.605$, $p = 0.037$). The results on instrument detection correlated...
Correlations of Electric Acoustic Stimulation Participants’ Mu.S.I.C. Test Results with Previous Musical Experience

Frequency of listening to music before HL correlated significantly negatively with the mean score for all 3 instruments on frequency discrimination ($r = -0.589; p = 0.044$). Correlations with other Mu.S.I.C. test results were not significant. Other indicators (playing an instrument in childhood, playing an instrument as an adult before HL, singing before HL) did not correlate significantly with Mu.S.I.C. test results.

Correlations of Electric Acoustic Stimulation Participants’ Mu.S.I.C. Test Results with Musical Activities after Implantation

Performance on instrument detection and instrument identification had a significant positive correlation with the number of reasons indicated for listening to music ($r = 0.604; p = 0.029$ and $r = 0.662; p = 0.014$, respectively) and the number of musical genres listened to ($r = 0.700; p = 0.008$ and $r = 0.679; p = 0.011$, respectively). There were no significant correlations of Mu.S.I.C. test results with other musical activities.

Discussion

One strength of this study is that 3 compatible groups were formed with factors known to influence music perception controlled between groups. Professional musicians were excluded from the study as it has been shown that they perform differently on music perception tasks [13, 14]. In order to separate effects of musical experience or training from CI or HA use, we carefully matched the groups according to their musical background. Age matching reduced effects of passive exposure to different types of music over time.

In our study, pitch perception was measured via a pitch ranking procedure. Loudness variations which might enable subjects to successfully rank the stimuli [15] were eliminated by equalizing all sounds to –3 dB.

CI users experience great difficulty on pitch-related tasks, as current users must extract the pitch information from either the temporal envelope or the spectral pitch associated with
electrode position [16]. To date, there are no published studies of pitch perception in EAS users. Fifty percent of our EAS participants reached a discrimination interval of 1 or 2 quarter tones, which is within the range of NH performance. One might assume that this could be attributed to residual low-frequency hearing. However, the results do not deteriorate significantly when the low-frequency hearing is blocked, although the fundamental frequencies of the stimuli then lie below the transmission range of the CI. If residual hearing were the decisive factor, one would expect a positive correlation between the natural hearing and the test result (which was not found) and that the pure tone would be affected less than the other stimuli. However, the opposite is true. Therefore, biological factors such as better neural survival must be taken into consideration. This probably allowed the EAS participants to make better use of the temporal information and spectral pitch transmitted via the CI, i.e., not only the overtones but also whatever information was transmitted by the CI when the pure tones were below CI transmission range.

Melodies with a distinctive rhythmic pattern are generally easier for CI users to identify and recognize [17–19]. Research has also shown that performance on melody recognition tests improves with lyrics present [20–22]. When asked to discriminate melodies from a melodic pattern only, unilateral CI subjects have been shown to perform much worse than NH subjects [23]. Gfeller et al. [9] observed that 4 subjects using the Nucleus Hybrid CI performed better than CI users on melody recognition without lyrics. Dorman et al. [24] and Kong et al. [25] describe better melody recognition on a melody pattern task (without rhythmic clues and lyrics) in subjects using a CI in one ear and an HA in the other (binaural) versus in the CI-only condition. Our EAS participants performed better than our CI participants on melody discrimination, though results were not statistically significant.

Chord discrimination, as another pitch perception task, is less challenging for unilateral CI users than other music perception tasks [23]. EAS users have even more success, as they can make use of the fundamental frequency information delivered by their HAs. Our CI participants’ good performance seems plausible, since chords generate a complex overall signal in the speech processor by overlapping several harmonic sequences. This signal is applied via several electrodes. The generated complex pulse pattern probably contains sufficient information to categorize similar sounds as ‘same’ or ‘different’.

Though results from many previous studies assessing rhythm discrimination are inconsistent, probably because of methodological differences [19], there seems to be overall agreement that CI users’ rhythm perception is similar to NH listeners’ [5]. In this study, we also found similar rhythm discrimination results for NH and EAS participants. Similar to the findings by Leal et al. [21] on unilateral CI users, we also did not find correlations between rhythm discrimination abilities and EAS participants’ musical activities or experience.

Another factor influencing the enjoyment of music is the ability to differentiate the quality of two tones of the same pitch played by different instruments, or timbre identification. Several studies report poor performance on instrument identification in CI users. This is still true for more modern CIs whose users vary widely in performance, both among subjects and across instrument types [5, 17, 23, 26–28]. Gfeller et al. [9] showed that the 14 EAS subjects tested performed better in high- and low-frequency instrument recognition than traditional CI users. Our results contrast with these data as our EAS participants’ performance on instrument identification did not differ from our CI participants’. However, the tasks in both studies are fundamentally different and Gfeller et al. [9] did not match subjects.

It has been reported that unilateral CI users have difficulty detecting the number of
instruments being played simultaneously during one piece of music [29]. Instrument detection was also difficult for the EAS participants in this study. It is noteworthy that both the EAS and CI groups had difficulty positively recognizing even one instrument (fig. 2).

For our EAS group, better scores in the CI-only condition seems to indicate an absent positive impact of the HA but a positive influence of residual hearing. This appears contradictory at first. The results may, however, be explained by two independent mechanisms. Good residual hearing, on the one hand, as mentioned in the previous discussion of pitch discrimination, may be associated with well-preserved auditory pathways and thus, with an effective use of the pulse patterns generated by the CI. This could explain the positive impact of residual hearing in the EAS participants’ CI-only performance. Alternatively, the missing significant improvement in the EAS condition could have been caused by the HA distorting the complex sound structure during amplification [30] or by interferences between acoustic and electric hearing. That this effect seems especially prominent in the timbre-based tasks could be due to the fact that for timbre discrimination, the first few milliseconds of a tone played are critical for identifying the instrument. Additionally, the transient responses of the two devices are different, causing even more confusion than hearing through a CI only [31].

In music psychology there appears to be general consensus that tonal consonance must be distinguished from musical consonance and that the latter refers to the quality of intervals in a musical context [32]. Tonal consonance is attributed to the interference associated with the general pattern of interaction of pure tones in the auditory system described by the critical bandwidth (defined as the frequency region over which acoustic energy is integrated in the ear) [33]. Perception of musical consonance, however, is also influenced by the immediate context, musical style, musical enculturation of the listener and other factors [34]. No data exist, to our knowledge, on dissonance rating for EAS users. Unilateral CI subjects are known to rate samples similarly to NH listeners [29]. EAS, CI, and NH participants in the current study rated dissonance similarly, suggesting EAS users habituate to the sound perceived in electric acoustic hearing.

Although there are some cross-cultural and developmental differences in emotions resulting from listening to music, strong emotional responses are reported and subjects judge the emotions of music quite consistently, regardless of musical training [35, 36]. For basic emotions such as ‘happy’, ‘sad’, ‘afraid’, and ‘angry’, the judgments are highly consistent [36]. Unilateral CI users are known to rate music on a ‘happy-sad’ scale similarly to NH subjects [37]. Our study found that this is also true for EAS users. One explanation for this would be good transmission of rhythm (tempo) through the CI.

Unlike previously reported Mu.S.I.C. test results of NH subjects [29] but similarly to previously reported Mu.S.I.C. test results of conventional CI users [29], the EAS participants’ Mu.S.I.C. subtest scores did not correlate with each other and also did not correlate with previous or present musical experience or age.

Future studies including a larger number of subjects are needed to build on the data collected here. In general, though, the music perception abilities of EAS users seem closer to NH listeners’ than to CI users’, indicating the importance of residual hearing for musical tasks. It is likely that other biological factors influence the outcomes for music perception in EAS users.
References


Acceptance and Fitting of the DUET Device – A Combined Speech Processor for Electric Acoustic Stimulation

Silke Helbig · Uwe Baumann

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Abstract

Background/Aims: Subjects with sufficient residual low-frequency hearing after cochlear implantation can benefit from electric acoustic stimulation (EAS). A combined speech processor (MED-EL DUET™), which incorporates a hearing aid and a speech processor in one device, was designed especially for this group of patients. The present report evaluates the influence of postoperative pure tone audiometric results on personal acceptance of the DUET system in EAS users. Method: Fifteen subjects underwent cochlear implantation for EAS and hearing preservation was achieved at least partially. All were fitted with the DUET EAS hearing system. Personal acceptance (measured by whether or not they were using the DUET system) in combination with audiometric results were investigated over time. Results: The combined processor was accepted by the majority of the subjects. However, those who had initial or further loss of residual hearing of more than 55 dB at 125 Hz or more than 70 dB at 250 Hz and 98 dB at 500 Hz rejected the DUET device. Conclusion: The combined processor enables subjects with sufficient hearing preservation in the low-frequency range up to 500 Hz to benefit from EAS. Acceptance is dependent on the pure tone audiometric outcomes after surgery and can vary with hearing loss progression.

Since the development of the principle of electric acoustic stimulation (EAS) in 1999 [1], EAS has been more and more widely used to benefit individuals with mild-to-moderate hearing loss in the low to mid frequencies, falling to a severe-to-profound hearing loss in the high frequencies [1–13]. In the earliest form of EAS (before the introduction of the combined processor), patients used a cochlear implant (CI) for electrically stimulating the high frequencies in the basal region of the cochlea and an in-the-ear (ITE) hearing aid in cases where additional acoustic amplification was necessary for the complete or partially preserved low-frequency range. In cases of nearly normal hearing thresholds in the low-frequency region some patients experienced a benefit even without using amplification.

The employment of two separate hearing prostheses on one ear was cumbersome for many early EAS users because: (1) handling of two aids with different types of batteries and battery life spans was tedious and (2) patients with poorer low-frequency thresholds were left with insufficient amplification, especially in the frequency region below 500 Hz.

Both of these reasons paired with the lack of sufficient amplification and wearing comfort sometimes resulted in discontinuing the use of the ITE hearing aid.
The introduction of the DUET™ in 2006 (MED-EL, Innsbruck, Austria) offered the combination of a hearing aid and a CI speech processor in one single device for the first time. While the hearing aid part is specially designed to achieve amplification in the low frequencies between 125 and 1,500 Hz, the mid and high frequencies are transmitted to the implant stimulator by the CI speech processor part of the device.

Though improvement in surgical procedure [5, 14–16] and development of very atraumatic electrode carriers [17, 18] allow a very high degree of hearing preservation, some patients experience partial or complete loss of residual low-frequency hearing, either initially or over time [12]. This fact can hamper the benefit of acoustic amplification and therefore, acceptance of the DUET device. The aim of the present study was to evaluate the acceptance of acoustic amplification in DUET EAS subjects depending on pure tone audiometric results.

### Materials and Methods

#### Subjects and Audiometric Assessment
We studied the acceptance of the hearing aid part of the DUET device in 15 subjects, 9 females and 6 males, who were fitted with an EAS hearing system after EAS surgery.

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Sex</th>
<th>Age at implantation years</th>
<th>Implant</th>
<th>Electrode</th>
<th>Side of implant</th>
<th>Postoperative interval months</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
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<td>1</td>
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<td>40</td>
<td>COMBI 40+</td>
<td>medium</td>
<td>right</td>
<td>115</td>
<td>aminoglycoside</td>
</tr>
<tr>
<td>2</td>
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<td>45</td>
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<td>left</td>
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<td>idiopathic</td>
</tr>
<tr>
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<td>medium</td>
<td>right</td>
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<td>idiopathic</td>
</tr>
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<td>standard</td>
<td>right</td>
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<td>idiopathic</td>
</tr>
<tr>
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</tr>
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</tr>
<tr>
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<td>FLEX^EAS</td>
<td>left</td>
<td>6</td>
<td>idiopathic</td>
</tr>
<tr>
<td>8</td>
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<td>COMBI 40+</td>
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</tr>
<tr>
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<td>33</td>
<td>COMBI 40+</td>
<td>standard</td>
<td>left</td>
<td>89</td>
<td>retinitis pigmentosa</td>
</tr>
</tbody>
</table>

Mean 54 49
The hearing aid component of the DUET speech processor is equipped with 4 trimming controllers designed for adjustment of gain, low-frequency slope (LFS), volume and automatic gain control (AGC) threshold. Gain at 500 Hz is adjustable between 27 dB HL and 42 dB HL, and peak maximum gain is 52 dB HL at 1.6 kHz. Above 2 kHz, no amplification is provided since this part of the speech spectrum should be transferred via the CI. The LFS can be set between 0 and 18 dB/octave. Sloping hearing thresholds should be fitted with a higher setting of this controller, whereas a flatter threshold requires a reduction of this parameter. The volume controller is responsible for an overall attenuation and serves a range between 0 db HL and –47 dB HL. Its intended use is to balance loudness between hearing aid and CI components. The fourth trimmer determines the AGC threshold between input levels of 40–70 dB HL.

Fitting of the hearing aid component was carried out according to the manufacturer’s fitting guide [19]. Amplification was set based on the hearing threshold at 500 Hz, applying the half-gain rule. LFS setting was calculated by subtraction of hearing thresholds at 250 and 500 Hz, and half of this difference determined the setting of the LFS trimmer. After setting of gain and LFS a coupler measurement was performed to control the hearing aid component fitting. Then, the CI component was activated in addition to the hearing aid component and a fine tuning of attenuation was individually carried out in order to balance loudness between both systems. Then, a loudness scaling test was performed at 500 Hz with the CI component deactivated. The objective of the loudness scaling test was to determine a setting of the AGC threshold using the designated trimmer.

Prior to setting of the hearing aid controllers, the fitting map of the CI component was modified to provide reduced overlap with the amplification of the hearing aid. Vermeire et al. [20] have shown that reduced overlap is beneficial across listening conditions. Frequencies with hearing thresholds worse than 65 dB HL were considered as crossover points and the filter setting of the CI component was set accordingly [9]. With larger overlap between the CI and hearing aid components, subjects with nearly normal hearing in the lower-frequency range complained of hearing an echo. Sometimes the amplification peak of the hearing aid component at 1,600 Hz led to problems in patients suffering from dead regions in that area (areas without any residual inner hair cells on the basilar membrane), because presumably neighboring functional inner hair cells with lower center frequencies were activated. In these rare cases, a distorted speech impression was reported. To improve speech quality, amplification was attenuated in affected subjects.

Device Fitting
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Results
At the end point of the present study, 11 of 15 subjects were still using combined EAS (DUET), while 4 (subjects 12–15) had rejected the acoustic amplification due to insufficient benefit and were using electric stimulation only. Mean pure tone audiometric thresholds of both groups – acoustic stimulation users and nonusers – are shown in figure 1. Within the frequency range up to 500 Hz, DUET users showed thresholds of a maximum of 75 dB HL at 500 Hz, while nonusers showed hearing loss down to 105 dB HL. Both groups revealed a maximum hearing loss higher than 120 dB HL for frequencies higher than 500 Hz. Speech audiometry results in the group of DUET nonusers revealed a mean outcome of 66% for monosyllable testing (fig. 2a) and 62% for sentence testing at a 10-dB signal-to-noise ratio (fig 2b).
Discussion

The present results show that subjects with residual hearing better than 75 dB in the frequency region of 500 Hz and below benefit from an EAS device. Furthermore, we can also say that it is very likely that subjects with a hearing loss of more than 55 dB HL at 125 Hz, 70 dB HL at 250 Hz, and 98 dB HL at 500 Hz will discontinue the use of the acoustic amplification part of the system.

The DUET EAS hearing system is designed to amplify acoustic hearing between 125 and 1,500 Hz by between 30 and 75 dB HL. These specifications match the indication criteria for EAS patients, who should present with hearing thresholds of at least 65 dB HL for frequencies up to 750 Hz. Average maximum gain of the device is about 40 dB for frequencies up to 1 kHz. In our investigation we found that amplification of acoustic hearing by the DUET device works well within this dynamic range, while postoperative initial or progressive hearing loss of more than 75 dB HL cannot be handled sufficiently.

Despite very careful surgical procedures [5, 14–16] and highly sophisticated electrode designs [17, 18] it cannot be guaranteed that residual hearing in the low frequencies will be preserved completely. Recent studies demonstrate complete hearing preservation (defined as a decrease of 10 dB HL or less) in 36% [21], 50% [17] and up to 67% [22] of the implanted subjects. Complete hearing loss is minimized, but implantation very often results in partial hearing loss either acutely or progressively. It can be assumed that initial loss is due to intracochlear damage during implantation, while slowly progressing hearing loss can be caused by factors such as new tissue formation within the cochlea [23].

Though the benefit of EAS has been proven by different study groups [1–13], some subjects have shown insufficient hearing thresholds postoperatively which were out of the range of the available acoustic amplification at the time and which sometimes complicated postoperative fitting. Current EAS hearing devices provide higher acoustic gain in the lower frequencies than previous combinations of a speech processor component and an ITE hearing aid, and they offer more convenient handling. This enhances the acceptance of the device as well as the outcomes in speech understanding and enables more subjects than before to use EAS [24, 25]. Nevertheless there are still individuals who choose not to use EAS even with its easier handling features, most likely because they have insufficient residual hearing. In our study, we showed that the frequencies of 500 Hz and below seem to be especially crucial for the acceptance of the DUET hearing system. Better thresholds than 55 dB HL at 125 Hz, 70 dB HL at 250 Hz and 98 dB HL at 500 Hz should be present for acceptance to be expected. Below that benchmark it is very likely that the device as well as the idea of EAS are rejected. The frequencies higher than 500 Hz did not seem to influence acceptance since all subjects – DUET users and nonusers – showed a drop in their pure tone audiometry within this frequency range to scores where amplification of the hearing aid part of the processor is insufficient. Though the frequency range at or below 125 Hz is not
Fig. 2. Speech audiometry results of the 4 subjects who rejected the DUET and use the OPUS 2 speech processor. a Mean results for Freiburger monosyllables were 66%. b Mean Hochmair-Schulz-Moser (HSM) sentence results at a 10-dB signal-to-noise (S/N) ratio were 62%.

Table 2. Pure tone audiometric results of DUET users (1–11) and DUET nonusers (12–15)

<table>
<thead>
<tr>
<th>Subject no.</th>
<th>Hearing thresholds, dB HL</th>
<th>125 Hz</th>
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<th>500 Hz</th>
<th>750 Hz</th>
<th>1,000 Hz</th>
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</table>
essential for speech perception, it does seem to have an influence on DUET use.

Despite rejecting the EAS mode these subjects were provided with sufficient speech perception in the CI-only mode, as demonstrated in figure 2. 360° insertion of the EAS electrode enabled this group to have this good result. Compared with results of other groups [26], our results are even better for monosyllable testing than in the average CI patient.

The results of this study should help to predict the outcomes for individuals who are eligible for EAS prior to surgery. Since in approximately half of the cases [17, 21, 22] we must expect postoperative hearing loss of more than 10 dB HL, it would be reasonable to choose subjects with hearing of 50 dB HL or better at 500 Hz and below. The higher frequencies did not influence the acceptance of the DUET. By slightly changing the indication criteria, we could more accurately predict that these individuals will obtain long-term benefit in difficult listening conditions as a result of the increased gain and improved user comfort offered by the DUET.

Conclusion

Our data on the acceptance of the DUET EAS hearing system in patients with low-frequency hearing after cochlear implantation surgery help to more accurately define the indication criteria. Since nowadays hearing preservation still cannot be guaranteed, patients should be chosen carefully. Thresholds below 55 dB HL at 125 Hz, 70 dB HL at 250 Hz and 98 dB HL at 500 Hz after surgery indicate that acceptance of the combined processor and belief in the concept of the EAS mode are unlikely. Ideally, preoperative residual hearing should therefore be better to increase the likelihood of later acceptance of the EAS hearing system. Once this is the case, we will have more patients reliably and predictably obtaining benefit from the acoustic low-frequency amplification provided by EAS.

References


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From Electric Acoustic Stimulation to Improved Sound Coding in Cochlear Implants

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Medical Electronics, Innsbruck, Austria

Abstract
Research into electric acoustic stimulation (EAS) indicates that performance improves when acoustic stimulation is added to electric stimulation in subjects with residual low-frequency acoustic hearing. Research further indicates that information from the voice fundamental frequency ($F_0$) region accounts for the majority of the added speech perception benefit with EAS. This implies that improved frequency coding in the low frequencies could hold great potential for improving performance with cochlear implants (CIs). Results with new speech coding strategies such as fine structure processing indeed indicate that with improved low-frequency coding, at least some of the benefits of EAS can be translated to regular CI users.

Electric acoustic stimulation (EAS) by means of a shallow insertion electrode is a new method for treating individuals with residual low-frequency acoustic hearing and severe to profound hearing loss in the mid to high frequencies. This approach was first suggested and evaluated by von Ilberg et al. [1]. Several studies have shown that with appropriately designed and inserted electrodes, acoustic hearing can be preserved in the majority of subjects [2–4] during cochlear implant (CI) surgery for EAS. However, it is not only hearing preservation that has a great influence on the performance of EAS users; it is also the fitting of the device. In the first part of this chapter, we will discuss the benefits of EAS in general as well as some fitting aspects to consider with the acoustic stimulation component. In the second part of the chapter, we will then discuss the implications of EAS to CI sound coding strategies.

The Benefits of Combined Electric and Acoustic Stimulation

In the earliest EAS subjects, the fitting of the hearing aid (HA) component and fitting for the speech processor of the CI were done separately. The best option for the HA was considered to be the smallest possible HA, i.e., an in-the-ear HA, so that the CI speech processor could be worn behind the ear. However, several problems arose from this arrangement: (1) the two devices worked independently; (2) each device was of a different size and had a different battery life; (3) the in-the-ear HAs used were working at their limits in the low frequencies, and (4) handling was complicated. Several potential EAS users refused to accept wearing two devices and many chose to use the CI only instead. These observations of low acceptance were confirmed
in a multicenter study [5] in 18 EAS users fitted with a conventional in-the-ear HA (Oticon Adapto-P, Oticon, Denmark) and the TEMPO+ speech processor (MED-EL, Innsbruck, Austria). Meanwhile, with the growing number of EAS users, there was an obvious need to create a comfortable, user-friendly combined device for these subjects. In November 2005, the first hearing system to combine a speech processor and HA, the MED-EL DUET system, was introduced to the market. In order to overcome the aforementioned issues, the DUET hearing system features a single microphone for the TEMPO+ speech processor (using the CIS+ strategy) and a two-channel HA (allowing 40 dB gain through 1,800 Hz) in one unit. In early EAS users, the separate HA and speech processor were fitted separately. The introduction of a combined device, however, underscored the need for optimized combined fitting of EAS subjects.

Vermiere et al. [6] assessed 4 EAS subjects with different experience levels on 8 different fitting settings. The study specifically investigated the effects of 3 parameters, i.e. HA amplification, frequency range of amplification (amplification range), and the lower limit of the electric frequency range (minimum electric frequency). The HA amplification was set based on the half-gain rule, or on the half-gain rule plus 6 dB, while the amplification range was set to cover all frequencies either with a threshold better than 85 dB HL, or with a threshold better than 120 dB. The minimum electric frequency was either set to 200 Hz (full frequency range) or it was set as obtained from an unaided audiogram at 50, 65 and 80 dB HL (reduced frequency range). The maximum electric frequency was set at the default value (8.5 kHz). For each condition, speech tests at different signal-to-noise ratios were obtained. For each parameter change, subjects had approximately 1 day to adjust. Throughout testing, the contralateral ear was plugged.

On average, in the DUET condition, best speech understanding was achieved with the minimum electric frequency set to 554 Hz. This means that the best speech scores on average were obtained for the minimum electric frequency set to 554 Hz. This means that the best speech scores on average were obtained for the minimum electric frequency set to the frequency at 65 dB HL in the audiogram. For the CI condition, best speech understanding was found with the average minimum electric frequency set to 430 Hz. With the full frequency range, 78% of subjects had poorer speech test scores in the DUET condition when compared to the reduced frequency range. The difference between the minimum electric frequency for the DUET condition and the CI condition was statistically significant. This highlights the importance of fitting the CI and HA component both at initial stimulation in order to reach best benefit in shorter time.

Lorens et al. [8] compared speech perception performance in 17 experienced adult EAS users with that of 22 experienced adult CI users. Both groups were matched for duration of hearing
Impairment (EAS group mean: 23.8 years; CI group mean: 19.3 years), age (EAS group mean: 43.2 years; CI group mean: 42.3 years) and gender. Subjects were programmed with the CIS+ speech coding strategy. The main difference in programming between both groups was that the EAS subjects used a minimum electric frequency as obtained from the unaided audiogram at 65 dB HL, similar to the study by Polak et al. [7]. The minimum electric frequency for CI subjects was set to 300 Hz. For both groups the maximum electric frequency was set to 8.5 kHz.

The EAS subjects performed significantly better than the CI subjects. The best speech test results were those in the best-aided (contralateral ear was unplugged) and DUET (contralateral ear plugged) conditions. The poorest results were obtained in the DUET HA-only condition. These data place the EAS subjects in an intermediate position between CI and normal-hearing groups. The authors concluded that the combination of an HA and a CI processor as realized in the DUET EAS system is beneficial for hearing in noise and quiet.

One possible explanation for the benefit of EAS as discussed above may obviously lie in a significant contribution of the remaining low-frequency hearing, and studies attempted to assess the amount of acoustic input needed in EAS. Zhang et al. [9] investigated the benefit of contralateral acoustic hearing as a function of the upper frequency limit of the acoustic signal. It is important to note here that the contralateral audiograms of these subjects match those of the EAS users in the studies discussed above so that the results are relevant to (ipsilateral) EAS. The results show that the main benefit from added acoustic stimulation is already obtained with the acoustic information limited to a 125-Hz low-passed signal. The authors conclude that information from the voice fundamental frequency ($F_0$) region accounts for the majority of the speech perception benefit when acoustic stimulation is added to electric stimulation.

Implications for Cochlear Implant Sound Coding Strategies

The above-discussed benefits of EAS suggest searching for possible modifications in sound coding strategies for CIs, aiming at transferring the benefits of EAS to regular CI users. In this context, we regard an EAS user as a CI user with improved frequency coding in the low frequencies via acoustic stimulation. The aforementioned research on EAS patients and simulation studies in normal-hearing subjects indicate that better frequency coding in a relatively narrow low-frequency region is sufficient to already allow EAS users to reap a large part of the benefit made possible by EAS. Thus, the key learning from EAS in this context is that better coding of pitch is the main factor behind the benefits of EAS.

With respect to sound coding strategies for CIs, this means that improved frequency coding in the low frequencies could hold great potential for improving performance with CIs. However, in using acoustic stimulation in the low frequencies, as in EAS (depending on the degree of hearing loss in this region), both the place code as well as the temporal code are superior compared to classical CI coding and probably more or less close to normal. In the normal-hearing ear, sound is coded in place (tonotopically) and in time (phase locking), depending on frequency. Low-frequency sounds are coded in both time and place, whereas high-frequency sounds are only coded in place. Place coding refers to the fact that the place of neural activation in the cochlea is a function of frequency. Temporal coding refers to the fact that the neural response phase locks to the sound so that the frequency of the neural response reflects instantaneous frequency, i.e. the fine structure of the sound.

The term ‘fine structure’ goes back to the mathematician David Hilbert who demonstrated that any (band-pass) signal can be decomposed into a slowly varying envelope (i.e. amplitude modulation) and a high-frequency carrier of constant
amplitude which he referred to as the fine structure of the signal [10]. With respect to hearing, it was shown that for the number of independent information channels available in CIs today, the envelope is the main information carrier for (English) speech, but the fine structure is the main information carrier for music and for sound localization [11]. In contrast, for tonal language perception, fine structure is the main information carrier and thus, the relative importance of envelope and fine structure for tonal language perception resembled that for English speech recognition rather than that for English speech recognition [12].

In CIs today, place coding is produced by using multicontact intracochlear electrode arrays, each electrode contact of which is associated with a certain frequency band of the sound thus presenting the information within that frequency band to a place in the cochlea specific to the (center frequency of the) frequency band. However, accurate and selective place coding in CIs is hampered both by an imperfect placement of the intracochlear electrode array with respect to the frequency allocation function in the normal-hearing ear, as well as by the broad electric fields produced by these electrodes leading to large overlap of neural populations excited by each electrode, i.e. large electrode interactions. The offset in place of stimulation can in principle be accounted for by assigning to each electrode contact a center frequency that corresponds to the cochlear place of the electrode contact, and the literature indicates that an offset in place can at least partly and in the long run be compensated by remapping processes within the subject’s auditory system. In contrast, electrode interactions constitute one of the most intractable problems in CIs, and any attempts to reduce electrode interactions by means of, for example, multipolar stimulation did – aside from potentially significantly increasing the power requirements of CIs – not lead to significant improvements in performance.

In contrast, improving the temporal code provided with CIs is technically more feasible. In classical, envelope-based coding strategies – like CIS and n-of-m-based strategies – in use for the last 15–20 years, the temporal code is mostly limited to envelope modulations which are qualitatively identical across channels and mainly code pitch frequency. These envelope modulations are a result of unresolved harmonics which exist in normal hearing at high frequencies only. It is well known in normal hearing that these pitch-related envelope modulations are only a relatively weak code for pitch and are not able to produce musical pitch.

There have been several attempts to improve sound coding in CIs by a frequency-dependent combination of classical envelope coding and explicit temporal coding. In 1991 already, Wilson et al. [13] investigated a strategy (PP/CIS) with fine structure coding on the most apical channel. The first commercially available coding strategy explicitly providing the fine structure of the sound signal in several frequency bands is the fine structure processing (FSP) strategy implemented in the OPUS family of audio processors by MED-EL. A similar approach has recently been proposed for a spike-based temporal auditory representation strategy in Grayden et al. [14].

The FSP strategy makes use of the FineHearing technology aimed at improving both the temporal and the tonotopic coding of sounds in CIs with particular emphasis on temporal coding in the low to mid frequencies. In contrast to the fixed-rate envelope-based coding strategies mentioned above, FineHearing uses the timing of stimulation to code the temporal structure of the sound. Based on EAS, channel-specific sampling sequences (CSSS) are used in the low to mid frequencies in an attempt to produce better temporal coding through improved phase locking. CSSS are a series of stimulation pulses which are triggered by zero-crossings in a channel’s band-pass filter output [15]. Thus the instantaneous repetition rate of these sequences equals the instantaneous fine structure frequency of the signal in the frequency range represented on that channel. Using these
sequences, better frequency information can thus be attained in the low to mid frequencies, where results with EAS indicate that fine structure information is particularly helpful.

Place coding is achieved by creating pitch percepts which are intermediate to the pitch percepts created by stimulating single electrodes in isolation using so-called virtual channels [16]. FineHearing technology uses band-pass filters with a bell-shaped frequency response allowing a smooth transition of stimulation from one electrode to the adjacent electrode thus producing pitches intermediate to the pitches perceived when one of these electrodes is stimulated alone.

In the FSP strategy, temporal coding using CSSS is provided on the first through third most apical channels (fig. 1). On the remaining channels, envelope-based coding is provided. Thus, the FSP strategy better represents normal hearing since the low frequencies are coded in both timing and place of stimulation, whereas high frequencies are coded in place of stimulation only. Results with the FSP coding strategy have been positive. A multicenter study recently conducted in Germany included 45 adult PULSARCI100 users who were switched over from the CIS+ strategy (as implemented in the TEMPO+ speech processor) to the FSP strategy (as implemented in the OPUS audio processors) [17]. Speech and pitch perception testing as well as a sound quality questionnaire were administered immediately after switch-over and after 3 months of FSP use. A retrospective questionnaire comparing everyday performance with FSP and CIS+ was conducted after 1 month of FSP use.

The results of this study demonstrated a statistically significant improvement in vowel perception in noise (+4.8%) as well as monosyllable perception in noise (+6.1%). Sentence understanding in noise was better on average with FSP, although the resulting improvement in speech reception threshold was not statistically significant. Results also demonstrate improved pitch perception, particularly in the low frequencies. Here, users could perceive low-frequency tones better with the FSP strategy than with the C40+ strategy. These results are consistent with those from the questionnaires. Both questionnaires indicate a strong preference for the FSP strategy.

These results are in agreement with other studies comparing FSP and CIS+. In a switch-over study from the TEMPO+ to the OPUS 1 or OPUS 2 speech processor, a significant advantage for FSP was found in numbers, monosyllables, and sentence perception in quiet and in noise after 8–12 weeks of FSP use [18]. After 1 year of FSP use, 8 of the subjects in this study were retested and showed a significant advantage for the FSP strategy over the CIS+ strategy in sentence perception at a 10-dB signal-to-noise ratio [19]. In a study investigating performance with the FSP strategy in long-term CI users, Vermeire et al. [20] found significantly better speech perception in noise after 12 months of FSP use when compared to the CIS+ strategy. In other studies, better perception of prosody information [21] and better instrument identification and melody discrimination where also demonstrated [22] for the FSP strategy.

Other studies investigated the effect of FineHearing technology on pitch perception in more depth. Mitterbacher et al. [23] found better pitch discrimination with the FSP strategy when using synthetic signals such as sawtooth and triangle waves, particularly in subjects who were poor performers. On average, just noticeable differences in pitch were 10 percentage points smaller with FSP than with CIS+ in these subjects. For pure-tone signals, Mitterbacher et al. [24] also found improved low-frequency pitch perception with the FSP strategy compared to the CIS+ strategy. Their results indicate that, at least for the most apical channel in a CI, place coding is impeded by the fact that this electrode does not have a more apical neighbor producing lower pitch – a problem which is inherent to place coding via virtual channels in general. In contrast, temporal coding in FSP succeeds in producing distinct
pitch percepts. For complex tones (wideband signals), similar results for FSP and CIS+ were found across the whole frequency range tested. This suggests that providing additional temporal information in FSP does not compromise the transmission of spectral cues when compared to CIS+. Similar results were found by Schatzer et al. [25]. With the FSP strategy, they found large improvements in pitch discrimination for low frequencies and a constant increase in pitch over a logarithmic frequency axis compared to CIS+. Subjects again demonstrated better pitch perception in the low frequencies with the FSP strategy.

Results with the FSP strategy discussed above are at least qualitatively in agreement with the few results reported for other strategies combining temporal and envelope coding in CIs. For the PP/CIS strategy, results are available from 1 subject [13]. Although no difference could be found in speech perception between PP/CIS and CIS, the authors mention that the PP/CIS strategy sounded natural, especially for music.

The results above show that a strategy providing a frequency-dependent combination of envelope and fine structure coding like the FSP strategy allows better pitch perception than a traditional envelope-based CIS-type strategy, at least for narrowband signals like pure tones. The results also indicate that both time and place coding complement each other in that if one of the two codes fails (e.g., the place code for the low frequencies in CIS+) then subjects can effectively use the other code to extract pitch information. Further, as discussed above, the results suggest that providing
additional temporal information does not compromise the transmission of spectral information. Providing both the time and place code should thus make frequency coding more robust in CIs. The literature suggests that each code should have its own specific advantages and weaknesses. In a large body of literature, the time code was shown to be very reliable; however, it currently seems to be restricted to frequencies below 300–1,000 Hz, depending on the subject [26, 27]. In contrast, the place code works across a wider frequency range (basically the complete cochlear region covered by the electrode). However, the number of intermediate pitches in a certain cochlear region should depend on subject-specific parameters such as neural survival and has been shown to vary largely across subjects, and across cochleas within subjects [28].

Conclusions

Research indicates that information from the voice fundamental frequency ($F_0$) region accounts for the majority of the added speech perception benefit with EAS, beyond the benefit of electric stimulation alone. This carries two important implications. First, residual acoustic hearing in a relatively narrow range in the low frequencies should be sufficient for making a subject a good candidate for EAS. Second, improved frequency coding in the low frequencies could hold great potential for improving performance with CIs. This approach is utilized by new speech coding strategies like the FSP strategy. Results with FSP indeed indicate that with improved low-frequency coding, at least some of the benefits of EAS can be transferred to regular CI users.

References

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Hearing Preservation Surgery: Current Opinions

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Abstract

Background/Aims: Although the indications and surgical technique for cochlear implantation are well formalized, the introduction of hearing preservation surgery and electric acoustic stimulation have posed new questions for the cochlear implant clinician. This study was designed to crystallize the contemporary views of the implant community on how best to implement these new strategies.

Method: An anonymized questionnaire was made available to members of the Politzer Society and a selected group of implant surgeons via the Internet. Five questions required the respondent to choose a specific answer from the text on technique and 17 questions assessed the relative importance attached to the statements relating to the surgical process. A final question inquired on what basis the opinions were derived. The country of origin was also identified.

Results: The questionnaire was sent to 180 clinicians of whom 62 replied (34%). Tacit agreement was obtained in 2 of the specific questions and in 10 of the relative importance inquiries. There were varying degrees of opinions on the remaining questions.

Conclusion: It is clear that there is still limited consensus between surgeons when considering ways of maximizing outcomes in hearing preservation surgery and electric acoustic stimulation. More protocol-driven studies are required before an accepted gold standard approach can be achieved.

The concept of combined electric and acoustic stimulation (EAS) for patients with profound sensorineural hearing loss who have undergone cochlear implantation has provided a focus of interest and research for over 10 years [1]. The ability to retain useful low-frequency acoustic hearing, whilst electrically stimulating the cochlea in the high-frequency range is thought to be associated with improved quantifiable patient outcomes.

This project aimed to collate the opinions of clinicians (level of evidence 5, Oxford Centre for Evidence-Based Medicine) [2] on their actual clinical practice in the selection and operative management of patients undergoing EAS surgery. There are a number of published operative approaches for EAS surgery with further stepwise refinements – all designed to preserve hearing and adequately stimulate the cochlea [3–5]. However, there has been no consensus considering the importance or significance of each management decisions. Changes in surgical technique have been based on intuitive assumptions with the causes of residual hearing loss still not fully understood.

During the early years of cochlear implantation emphasis was on implanting a safe and reliable electrode array into the bony cochlear cavity. Entrance was obtained via the round window (as the reliable landmark) but the size and shape of the devices and the hook region of the cochlea led to difficult insertions. The safer and easier option became a bony cochleostomy placed antero-inferior to the round window, which could be fashioned to receive the different commercially available electrode options. A subgroup of implant
candidates began to appear with severe hearing disability yet retaining thresholds to pure tone testing in the low frequencies. Traditional criteria often excluded these patients from implantation. Taking into consideration the frequency-specific nature of the cochlea (the apex covers low tones, the base high tones) partial insertion was considered with a view to preserving acoustic hearing in the low tones which could then be stimulated by acoustic amplification [1]. Unfortunately the first generation of ultrashort electrodes was associated with insufficient electric stimulation and poor outcomes although acoustic hearing could be preserved [6]. Such an impetus led to the development of electrode arrays characterized by their soft and flexible design and of a length perceived to give adequate electric stimulation [7]. Although some of the arrays had been designed as perimodiolar so as to minimize current spread to the adjacent neural material and preserve battery life, they were shown to be more traumatic to the cochlea [7] and so straight arrays that would lie along the outer wall were introduced. Alongside these developments the technique of electrode array implantation was re-evaluated under the banner of soft surgery. It was perceived that a bony cochleostomy might impart significant trauma to the cochlea and in the majority of cases, the round window approach was reconsidered as the preferred route. By meticulous dissection, the round window membrane could be visualized in its greater entirety with little or no morbidity, to the surrounding structures, even in children [8]. The prospect of an acute endocochlear inflammatory reaction from infection and trauma was considered firstly with the introduction of prophylactic antibiotics, systemic and then local, and for trauma corticosteroids, again systemic and local. Contamination of the perilymph during insertion was avoided by guarding the array in a protective sleeve. Sealing of the cochleostomy site was achieved with a simple fat plug by some and augmented with fibrin glue by others. On CT scanning, Fraysse et al. [9] computed the cochlear size to obviate overinsertion in small cochleae (resulting in trauma) and underinsertion in large cochleae (inadequate stimulation). Other groups [3] wished to assess electrode position in order to correlate electric stimulation to the frequency base of the neural template using the Greenwood map [10]. However, these processes provide clinicians with continuing dilemmas as differentiating the effect of each process is not possible with the limited patient pool.

**Method**

A qualitative assessment of the current opinion on hearing preservation and the provision of EAS was undertaken using an online questionnaire. Three email databases provided the basis for the subject pool under examination. The first list was the current members of the Politzer Society and the other two were from lists of international specialist surgeons provided by the implant companies MED-EL and Advanced Bionics Corporation. An online questionnaire was chosen for ease of communication. The questionnaire incorporated 23 questions. Using a 5-point Likert scale, subjects were asked to rank the importance of various steps and options a surgeon may undertake prior to and during cochlear implantation. Five questions focused directly on the variation and the operator’s preference in specific key surgical steps, whilst the final question inquired from what basis and understanding the subjects made their decisions. An introductory email was sent to all subjects with a link to the survey created using surveymonkey.com (www.surveymonkey.com, Seattle, Wash., USA). The questionnaire was conducted over a 13-month period to allow the subjects time to reflect and post responses. Non-responders to the original email invitation were contacted every 4 months to maximize survey numbers and thus the power of the findings. Only full responses were included in the final data set. The response data were transferred into Excel (Microsoft Corporation, Redmond, Calif., USA) for analysis.

**Results**

In total, there were 62 responses [out of a possible 180 (34%)], with no one repeating the survey. Respondents were from 22 different countries, with 5 respondents not listing their country.
Table 1 shows respondents per country. Seventy-seven per cent of the respondents reported that they answered the questionnaire from clinical experience, 13.1% from the literature and clinical meetings and 9.8% from intuition.

Two questions were posed about pre-operative criteria for selecting an individual for EAS surgery. The first considered the pure tone audiogram: 18% of respondents thought the pure tone threshold in quiet at 500 Hz was at least 40 dB,
32.8% thought it should be 50 dB, 24.6% favoured 60 dB, whilst 24.6% opted for 70 dB. Similarly, respondents were asked what percentage the monosyllable scores should be less than (with percentage of responses in parentheses): 30% (14.8%), 40% (52.5%), 50% (52.5%) and 60% (6.6%). Responses to each statement about a specific process in the surgery are shown in table 2. Respondents had to note if the process was not important at all, somewhat unimportant, neutral, somewhat important, very important, or whether they were unsure. A few questions did not have this response system, and are detailed here. The depth of insertion should be no deeper than 10 mm for 16.4% of respondents, 15 mm for 23%, 18 mm for 44.3% and 21 mm for 16.4%. Well over half of respondents (54.10%) felt the electrode should lie next to the modiolus, 31.1% thought it should lie in the scala media and 14.8% thought it should lie laterally in the scala tympani. Finally, when viewed radiologically, respondents answered that the electrode should not have passed around the cochlea more than 360° (58.5%), 320° (24.5%), 280° (17%) and 240° (6.6%).

**Discussion**

Answers from 62 respondents to a survey about opinions on hearing preservation surgery in EAS are detailed in this paper. It is evident from the responses that there are some clear points of consensus on certain steps in the surgical process on the one hand, and some clear areas of disagreement on the other.

Consensus was achieved on 10 points of the surgical procedure; most respondents noted the statements to be somewhat or very important. The greatest consensus was achieved for the statement ‘There should be minimal suction at the cochleostomy site’, reflecting the thought of keeping trauma to the inner ear to a minimum and limiting the loss of perilymphatic fluid. Other points of consensus were: (1) providing systemic antibiotics to be given peri- and postoperatively; (2) centring the cochleostomy 1 mm anterior-inferiorly to the horizontal midline of the round window and that it should be small; (3) that the endosteum should be kept intact and it, or the round window should be incised using a sharp instrument; prior to this, bone dust should be flushed from the mastoid and middle ear with Ringer’s solution; (4) the electrode array should be inserted slowly, and immediately following insertion, the cochleostomy should be sealed with connective tissue and fibrin glue. Finally, over half of respondents agreed that the electrode should go into the cochlea no further than 360° or one full turn, with the remainder saying it should be less – but all agreeing that any further would probably cause loss of hearing.

Both questions covering audiological preselection criteria showed some lack of consensus – with a range of opinions as to what decibel levels one should consider at 500 Hz and what the maximum monosyllable score in the best-aided condition should be. Perhaps this reflects uncertainty about what level will provide benefit versus the risk of hearing loss. The Cochlear standpoint (Hybrid for Professionals Brochure, 2008) states the maximum hearing loss should be 60 dB at 500 Hz and is less specific about the monosyllable scores, stating they should be between 10 and 60%. MED-EL (EAS Candidacy Sheet, 2008) reports the maximum hearing loss to be 65 dB at 500 Hz – showing minimal variation compared to Cochlear’s status, but both are lower levels than seen in the survey. The largest number of respondents (32.8%) thought the level at 500 Hz should be 50 dB. MED-EL’s statement on monosyllable scores is ≤60% at 65 dB SPL in the best-aided condition, whereas very few felt 60% was an acceptable monosyllable score – most favouring 50% (52.5%). The next point of pre-operative disagreement is whether radiological measurement of the cochlea size is needed. Thirty-four per cent of respondents said it was very important and 23% thought it was not important at all, with a spread of responses in between. This is interesting
<table>
<thead>
<tr>
<th>Statement</th>
<th>Not important at all, %</th>
<th>Somewhat unimportant, %</th>
<th>Neutral, %</th>
<th>Somewhat important, %</th>
<th>Very important, %</th>
<th>Not sure, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>As cochleae are of different sizes, radiological measurement of the size is needed</td>
<td>23</td>
<td>8.2</td>
<td>16.4</td>
<td>14.8</td>
<td>34.4</td>
<td>3.3</td>
</tr>
<tr>
<td>Systematic antibiotics should be given peri- and postoperatively</td>
<td>6.6</td>
<td>4.9</td>
<td>6.6</td>
<td>26.2</td>
<td>52.5</td>
<td>3.3</td>
</tr>
<tr>
<td>The middle ear cavity should be flushed with a non-aminoglycoside antibiotic solution</td>
<td>37.7</td>
<td>11.5</td>
<td>13.1</td>
<td>24.6</td>
<td>11.5</td>
<td>1.6</td>
</tr>
<tr>
<td>Prior to cochleostomy give a single intravenous dose of corticosteroid</td>
<td>6.6</td>
<td>14.8</td>
<td>14.8</td>
<td>32.8</td>
<td>27.9</td>
<td>3.3</td>
</tr>
<tr>
<td>Introduce the electrode array through the round window if possible</td>
<td>11.5</td>
<td>14.8</td>
<td>13.1</td>
<td>34.4</td>
<td>21.3</td>
<td>4.9</td>
</tr>
<tr>
<td>OR/IF NOT: The cochleostomy should be centred approximately 1 mm anterior-inferiorly to the horizontal midline of the round window</td>
<td>1.6</td>
<td>0</td>
<td>9.8</td>
<td>24.6</td>
<td>62.3</td>
<td>1.6</td>
</tr>
<tr>
<td>The cochleostomy should be small, no more than 1 mm in diameter</td>
<td>1.6</td>
<td>4.9</td>
<td>8.2</td>
<td>37.7</td>
<td>47.5</td>
<td>0</td>
</tr>
<tr>
<td>Expose the endosteum but keep it intact</td>
<td>0</td>
<td>8.2</td>
<td>1.6</td>
<td>34.4</td>
<td>55.7</td>
<td>0</td>
</tr>
<tr>
<td>Flush bone dust from the mastoid and middle ear with Ringer’s solution</td>
<td>3.3</td>
<td>4.9</td>
<td>8.2</td>
<td>24.6</td>
<td>59</td>
<td>0</td>
</tr>
<tr>
<td>Incise the endosteum or round window membrane using a sharp instrument</td>
<td>1.6</td>
<td>3.3</td>
<td>11.5</td>
<td>32.8</td>
<td>50.8</td>
<td>0</td>
</tr>
<tr>
<td>Place a drop of steroid solution at the cochleostomy site</td>
<td>16.4</td>
<td>19.7</td>
<td>21.3</td>
<td>24.6</td>
<td>11.5</td>
<td>6.6</td>
</tr>
<tr>
<td>Place a drop of hyaluronic acid (Healon) to cover the cochleostomy</td>
<td>9.8</td>
<td>6.6</td>
<td>21.3</td>
<td>32.8</td>
<td>27.9</td>
<td>1.6</td>
</tr>
<tr>
<td>There should be minimum suction at the cochleostomy site</td>
<td>0</td>
<td>1.6</td>
<td>0</td>
<td>9.8</td>
<td>88.5</td>
<td>0</td>
</tr>
<tr>
<td>Use a sheath or insertion tube to avoid contamination of the electrode array by blood or bone dust</td>
<td>8.2</td>
<td>19.7</td>
<td>29.5</td>
<td>24.6</td>
<td>13.1</td>
<td>4.9</td>
</tr>
<tr>
<td>The electrode array should be inserted slowly</td>
<td>0</td>
<td>1.6</td>
<td>16.4</td>
<td>23</td>
<td>55.7</td>
<td>3.3</td>
</tr>
<tr>
<td>Following insertion immediately seal the cochleostomy with connective tissue and fibrin glue</td>
<td>3.3</td>
<td>4.9</td>
<td>9.8</td>
<td>24.6</td>
<td>57.4</td>
<td>0</td>
</tr>
<tr>
<td>The frequency allocation to the electrodes should reflect their Greenwood location in the cochlea</td>
<td>6.6</td>
<td>8.2</td>
<td>39.3</td>
<td>18</td>
<td>19.7</td>
<td>8.2</td>
</tr>
</tbody>
</table>
considering that all agree that the electrode should not go further than 360° into the cochlea – so how can this be determined? Pre-implant high-resolution CT-based prediction is feasible and accurate when aiming for insertion depths of up to 360° [11] and is recommended as a procedure [12].

Despite some points of agreement regarding the surgical process, there were a number of points of disagreement. The first was on whether the middle ear cavity should be flushed with a non-aminoglycoside antibiotic solution. While 37.7% said this was not important at all, 24.6% said it was somewhat important. There is no real evidence in the literature of the value or not of this procedure, which suggests the need for further research.

The issue of providing a single intravenous dose of corticosteroids led to various responses. This is reflected in the literature – one study reported 20 of 27 cases receiving corticosteroids at or before preparation of the patient for surgery [9], while others reported postoperative provision [13] and two papers mentioned provision during surgery [14, 15]. Respondees were very divided regarding placing a drop of steroid solution at the cochleostomy site; this is only encouraged by one group of surgeons following the same surgical procedure [3, 12, 15, 16] and the results probably reflect a need for further research into the benefits of this. Whether to use Healon® to cover the cochleostomy also produced some uncertainty, despite reports of many surgeons doing this [3, 9, 12–14]. This is interesting, considering a publication [17] demonstrating that Healon reduces trauma, enables easier, deeper insertion of the electrode array, does not affect the spiral ganglion cell count and avoids contamination of the perilymph.

Placement of the electrode array according to the Greenwood location [10] in the cochlea also resulted in a spread of responses, with the greatest response being neutral. There is little in the literature to support or negate this, and it seems that pre-operative radiological evaluation may be more important. One surgeon suggested using the Greenwood map to determine insertion depth, though did acknowledge that pitch perception from electric stimulation may be lower than expected from the Greenwood map [12]. There is a little controversial discussion in the literature where some disagree that an electrode placed in the cochlea based on the Greenwood map would actually stimulate neurons tuned to that frequency [21, 22].
One final point where there is not complete consensus is whether to introduce the electrode array through a cochleostomy or through the round window. Just over 34% said round window insertion was somewhat important, 21% said it was very important and the rest was spread across responses. Round window insertion does seem to be the insertion method currently in favour in the literature – showing less trauma in histological studies [7, 8] and excellent hearing preservation outcomes [5]. However, some caution against this technique – as visibility of the round window may not be clear [23].

Conclusion

Although there is consensus on nearly half of the surgical steps required for preserving hearing in cases where the individual may have a significant amount of low-frequency hearing, there are still many steps that need to be further investigated before a clear procedure emerges. This becomes important as more potential candidates for EAS are seen in clinics worldwide, and surgeons aim to have as high a preservation rate as possible, to allow these individuals best use of their remaining low-frequency hearing.

References


Minimizing Intracochlear Trauma during Cochlear Implantation

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Abstract

Several clinical trials have now demonstrated the feasibility and benefit of ipsilateral bimodal electric and acoustic stimulation of the auditory system for patients with varying degrees of hearing loss. Surgical techniques employed as a part of these investigations have been similar and focus on the implementation of atraumatic surgical principles. Each procedural step aims at minimizing intracochlear damage. A cochleostomy site inferior and slightly anterior to the round window membrane forms the basis for creating an opening into the scala tympani that avoids the critical structures of the inner ear. Electrode arrays have also been developed and refined to allow for relatively limited insertion-related damage. Using these specialized approaches, hearing preservation rates approaching 90% have been achieved. While impressive, this number reflects the conservation of only some degree of residual hearing. Complete preservation of hearing without any loss in pure tone thresholds and/or discrimination abilities remains unusual, especially in subjects that have received a full-turn insertion. Thus, further work is clearly needed to optimize surgical protocols in an attempt to achieve total hearing preservation in all cases. A variety of biological and technological areas of investigation hold promise for fulfilling these goals. This report will review the current state of hearing preservation cochlear implantation as it relates to combined ipsilateral bimodal or electric acoustic stimulation.

Modern cochlear implants have evolved dramatically over the last decades. Current devices commonly provide adequate auditory information for verbal communication although hearing in noise and music perception remains relatively poor. Part of the reason why cochlear implant performance remains below that of normal-hearing individuals is the fact that before the acoustic input can be represented to the cochlear nerve electrically, it has to undergo substantial processing that can effectively reduce the delivered information to the auditory system. Direct electric stimulation of the spiral ganglion requires a very compressed dynamic range of only 10 dB or less as compared to over 100 dB in the healthy ear. Also, the signal has to be split into its spectral components in an attempt to mimic the tonotopic organization of the cochlea. Other speech-processing algorithms modify but may further downgrade the signal to maximize the effect of electric stimulation. Moreover, because the optimal electric stimulation strategy and method has yet to be determined, further losses of information are also probable at the site of neural excitation. Naturally, this loss of information along the cochlear implant stream reduces hearing for implanted patients well below that of normal-hearing individuals.

Several attempts are currently under way to improve hearing results with cochlear implants.
One approach is to use a combination of a person's natural hearing abilities (i.e. acoustic hearing) with direct electric stimulation of the cochlear nerve by way of a cochlear implant in the same ear [1, 2]. In its current format, electric stimulation is used in the basal cochlear regions to generate high-frequency percepts while the residual low-frequency regions of the cochlea are acoustically amplified by way of a conventional hearing aid. While these patients' low-frequency residual hearing abilities are typically insufficient when used alone, the addition of electric stimulation with a cochlear implant can provide supplementary information that broadens both the spectral and temporal auditory information delivered to the level of the brain.

Multiple clinical and basic science reports have investigated the feasibility of combining electric and acoustic hearing [3–9]. Early clinical data demonstrated that the combination seemed to improve hearing results in difficult listening situations such as background noise [2, 10, 11]. Since background noise has remained a significant impediment for conventional cochlear implantation users, the additional surgical efforts needed to preserve residual cochlear function appear to be justified. Based on these studies, a variety of techniques are being explored to maximize the outcomes of combining electric and acoustic stimulation.

The single most important prerequisite for providing both electric and acoustic stimulation in the same ear is the preservation of acoustic hearing following the surgical procedure. Prior to the institution of hearing preservation surgical techniques, reports demonstrated some postoperative hearing remnants in the implanted ear in up to 50% of conventional cochlear implant recipients [12]. Since the time of these reports, it was further hypothesized that by adapting less traumatic surgical principles, greater degrees of residual hearing could be preserved more frequently [13]. Further refinements in surgical technique and less traumatic electrode arrays used in the electric acoustic stimulation trials demonstrated even greater degrees of hearing conservation [5, 6]. In fact, several clinical studies have now shown that at least some hearing can be preserved in roughly 90% of cases [4, 7, 10, 11, 14–17]. Nonetheless, complete preservation of preoperative hearing abilities is only possible in roughly 50% of individuals, thus leaving much room for improvement.

This report will summarize current protocols and outcomes of hearing preservation cochlear implantation. Recent research also suggests that candidates without residual hearing might benefit from atraumatic cochlear implantation through preservation of critical neural elements within the cochlea and spiral ganglion.

**Possible Mechanisms of Hearing Loss**

The etiology and mechanisms responsible for cochlear implant-related hearing loss remain mostly unknown. With this in mind, a theoretical approach to preventing hearing loss related to cochlear implantation has been adopted. That is, the surgical practices and principles that are being used clinically have limited proof of effectiveness. It is clear that both immediate and delayed types of hearing loss have been identified following attempted hearing preservation cochlear implant surgery. It can be presumed that immediate loss of hearing would be the result of acute traumatic disruption while delayed losses result from reactive mechanisms to the surgical insult. Some of the potential mechanistic explanations are outlined below:

1. **Traumatic or immediate**
   - **Middle ear**
     1. Effusion
     2. Tympanic membrane perforation
     3. Ossicular fixation or disruption
   - **Inner ear**
     1. Vibratory injury to the inner ear (i.e. drilling on ossicles)
2 Opening of the cochlea (cochleostomy)
   a Perilymph fistula or suctioning
   b Periosteal/liquid-conductive injury (drill on periosteum or perilymph)
   c Direct injury to inner ear
      i Soft tissues (spiral ligament, stria vascularis, basilar membrane, organ of Corti, Reissner's membrane, etc.)
      ii Osseous structures (osseous spiral lamina, modiolus, Rosenthal's canals, etc.)
   d Electrochemical gradient disruption
   e Inner ear conductive (third window)
3 Electrode insertion
   a Perilymph displacement ± implosive or explosive injury
   b Direct inner ear damage
      i Soft tissues
      ii Osseous structures
4 Postinsertion-related hearing loss
   a Disruption of middle ear conductive mechanisms related to electrode array
   b Inner ear-related loss
      i Perilymph fistula
      ii Inner ear mechanical
      iii Toxic injury (blood, electrode materials, irrigation, etc.)
5 Progression of primary hearing loss pathology
   Currently, several hearing preservation protocols are under clinical investigation. Each protocol attempts to implement procedures that minimize both immediate and delayed mechanisms as outlined above. Specifically, atraumatic approaches and electrode insertions have been proposed that aim at minimizing the surgical aspect of intracochlear trauma. Nonsurgical measures such as the concomitant application of steroids should enhance tissue tolerability and thus reduce intracochlear damage on a cellular level.

Device Selection and Electrode Arrays

A variety of approaches have been considered for the preservation of residual hearing for the purposes of combined bimodal stimulation in the same ear. One such early approach was to use an extracochlear electrode array. While this procedure was highly successful at preserving hearing, the benefit of electric stimulation with this device was limited.

As with conventional cochlear implant patients, intracochlear implantation of multi-electrode arrays has been the predominant approach for achieving combined electric and acoustic stimulation. The ability to provide tonotopic, multifocal stimulation certainly appears to offer the promise of greatest performance. Theoretically, electric stimulation would be used for the anatomic regions of the cochlea that are no longer acoustically active because of organ of Corti loss. Since high-frequency, sloping sensorineural hearing losses have such findings in the basal region of the cochlea, arrays advanced into this segment would initially contact the area of interest. Surgically, this anatomic-pathological situation is fortuitous.

In designing these devices, divergent goals have become evident. From a hearing preservation standpoint, short electrode arrays reduce the risk...
to residual acoustic hearing by limiting the possibility for intracochlear trauma from the insertion. On the contrary, short arrays can only access limited numbers of neural elements, thereby reducing the spectrum of neural excitation. Depending on the residual hair cell and neural populations present in a particular ear, significant spectral gaps might exist between the acoustic hearing abilities of the ear and the neural elements that are being stimulated. Deeply inserted electrodes might provide for unnecessary electric-acoustic overlap and/or impair local regions of acoustic activity. Finally, if hearing were lost from a short electrode insertion, this device might prove ineffective when compared to a conventional, full-length cochlear implant. From a tonotopic perspective, one could envision the ideal electrode array placement to be just deep enough to cover only those areas where the acoustic mechanism has been lost.

A variety of studies have been carried out using human temporal bones to assess the insertion characteristics and collateral damage caused by electrode insertion. What is clear from these studies is that small, flexible arrays that result in a smooth insertion are critical for avoiding cochlear trauma. Deeply inserted arrays, on the other hand, are associated with an increased risk of intracochlear trauma, especially those inserted beyond one full turn (fig. 1d) [18]. Spiral ligament avulsion, basilar membrane disruption and osseous spiral lamina fractures have been seen in these bones. These lesions can not only result in loss of residual hearing but can also reduce the available neural substrate. Loss of neural integrity could have severe consequences on performance potential.

The manufacturers involved in hearing preservation cochlear implant surgery for the purposes of combined stimulation have taken very different philosophical approaches in designing their electrode arrays as described above. Cochlear Corp.’s (Melbourne, Australia) Hybrid Device uses a very short electrode array that covers only 10 mm (6 mm in the initial phase of the trial) of cochlear length with the intent of maximizing hearing preservation. While results do suggest that this device is very good in this regard, prolonged acclimatization is needed. This delay in performance may be due to the aforementioned spectral gap induced by using such a short array. Nonetheless, time seems to overcome this shortcoming and patients with greater degrees of residual hearing can be implanted because of the safety of this device.

MED-EL Corp. (Innsbruck, Austria) has taken a very different approach when producing their device for electric acoustic stimulation. They use a longer array in an effort to avoid both the spectral gap as well as to insure that patients that have lost their hearing from the surgical procedure have the benefit of a full-length, conventional cochlear implant (fig. 2) [11]. While this approach most likely obviates the need for further surgery to replace an electrode that was insufficient for electric stimulation alone, the frequency of hearing loss from this device has been somewhat greater. This manufacturer has more recently produced an array with increased flexibility in an effort to reduce the hearing loss rate and ongoing clinical trials seem very promising (fig. 3) [19]. The modified electrode array features a reduced contact spacing of 1.9 mm, which results in insertion depths of roughly 22 mm when the most basal contact pair is at the cochleostomy. Table 1 summarizes the hearing preservation rates among the various clinical trials and devices.

### Surgical Technique

#### Approach to the Cochlea

The initial surgical descent to the cochlea might be the least important aspect of hearing preservation surgery. Noise trauma via high-speed otologic drills, for example, has been discussed as a possible factor. Both pneumatic and electric drills have been used for decades in chronic ear surgery without causing clinically significant sensorineural hearing loss. The more vulnerable nature of
the hearing-impaired inner ear might pose an additional risk. Overall, however, evidence suggests that this might be clinically insignificant [20].

**Access to the Scala Tympani**

Recent efforts to preserve residual hearing have prompted a multitude of publications on correct cochleostomy placement. Historically, the round window itself was utilized to access the scala tympani. Then, relatively stiff multichannel electrode designs required a straight insertion trajectory avoiding the cochlear hook region. Also, a cochleostomy typically bypasses the often times problematic anatomic alignment of the round window membrane. It was then proposed that by drilling the promontory bone, one could reliably gain access to the intracochlear lumen. This procedure has been generally known as the cochleostomy.

Recent cadaveric histological temporal bone experiments demonstrated substantial intracochlear trauma in the region of the cochleostomy despite the application of soft surgical techniques.

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**Fig. 1.** Histological evaluations of various electrodes and insertion techniques. 

- **a** MED-EL Flex EAS electrode in the scala tympani (ST) of the middle cochlear turn. The electrode assumes a position along the lateral wall of the cochlea. 
- **b** Cochlear Corp. Contour Advance electrode assuming a perimodiolar position in the middle cochlear turn. No intracochlear trauma visible. 
- **c** Iowa Hybrid electrode (Cochlear Corp., 10 mm in length) inserted via a superior cochleostomy into the scala vestibuli (SV). Implantation into the scala vestibuli is typically associated with substantial intracochlear trauma and should thus be avoided. 
- **d** MED-EL Standard electrode deeply implanted into the cochlear apex resulting in substantial apical trauma. Also, buckling of the basal portion of the electrode generally causes fractures of the osseous spiral lamina as demonstrated herein.
This prompted several anatomical reviews closely studying the morphology of the basal cochlear turn and its implications for cochlear implantation [21, 22]. From those studies, it became clear that the lateral attachment of the spiral ligament often interferes with a promontory cochleostomy thus resulting in intracochlear trauma. By using the round window as a surgical landmark, on the other hand, the access route to the scala tympani becomes less arbitrary. Several locations around the round window have been described. A recent histologically controlled insertion study has demonstrated that a cochleostomy location inferior and only slightly anterior to the round window resulted in virtually no basal cochlear traumatization (fig. 4) [23]. A cochleostomy location more anterior, however, was shown to damage the lateral attachment of the spiral ligament in many cases.

Electrode insertions through the round window itself might be safe as well [22, 24]. From anatomic studies, it seems that a cochleostomy abutting the round window membrane might in fact be the best option allowing for a relatively straight insertion trajectory in combination with the advantage of using the round window as a proper surgical landmark to locate the scala tympani. Hence, the advantages of a cochleostomy and a round window insertion are combined (fig. 5).
shows histology from two frequently used cochleostomy locations).

In most temporal bones, the round window cannot be directly viewed until its bony overhang has been properly removed. Commonly, a maximized facial recess is required to gain adequate access to the hypotympanum and the round window region. Maximizing the facial recess puts the chorda tympani at higher risk than usual. Also, drilling the bony overhang might affect the structural integrity of the round window membrane. Hence, perilymph might leak prematurely possibly resulting in lower hearing preservation rates.

Intracochlear blood mainly from middle ear mucosal dissection might be another source for inner ear toxicity and therefore hearing loss. However, clotted blood has been safely used for decades to seal the vestibule during stapedectomy. Also, intra- and perilabyrinthine use of the suction should be avoided and a small suction tip should be used to assure safe dissection near the round window. As with intralabyrinthine blood, suction trauma has been intentionally applied by many surgeons in the past without causing permanent sensorineural hearing loss. Hence, the significance of the atraumatic use of the suction

| Study and device | Electrode manufacturer | insertion depth | position
|----------------|----------------------|----------------|--------|
| 1999 von Ilberg et al. [1] | MED-EL | approx. 20 mm | antimodiolar
| 2003 Skarzynski et al. [3] | MED-EL | approx. 20 mm | antimodiolar
| 2004 Gstoettner et al. [5] | MED-EL | 18–24 mm | antimodiolar
| 2004 Kiefer et al. [6] | MED-EL | 19–24 mm | antimodiolar
| 2004 Gantz and Turner [8] | Cochlear Corp. | 6–10 mm | antimodiolar
| 2004 Meller et al. (personal communication) | MXM | NA | extracochlear
| 2005 Gantz et al. [10] | Cochlear Corp. | 6–10 mm | antimodiolar
| 2005 James et al. [17] | Cochlear Corp. | 17 mm | perimodiolar
| 2006 Gstoettner et al. [15] | MED-EL | 18–24 mm | antimodiolar
| 2006 Gantz et al. [7] | Cochlear Corp. | 6–10 mm | antimodiolar
| 2006 Fraysse et al. [16] | Cochlear Corp. | 17 mm | perimodiolar
| 2007 Skarzynski et al. [14] | MED-EL | approx. 20 mm | antimodiolar
| 2007 Skarzynski et al. [14] | MED-EL | approx. 20 mm | antimodiolar

ITE hearing aid = In-the-ear hearing aid; CNC = Consonant nucleus consonant word discrimination test; AOS = Advance offstylet electrode insertion technique.
remains unclear, although at this point all steps should be employed to guarantee best results. Also, previous evidence from stapes surgery can only be viewed as inconclusive and might not apply since the site for the inner ear opening is quite different.

**Insertion Trauma**
A variety of mechanisms are believed to carry the potential to cause intracochlear trauma during the electrode insertion process.

**Endosteal Injury.** Trauma to the endosteum will increase postoperative fibrosis and osteoneogenesis. We have not been able to demonstrate significant endosteal injury in temporal bones, either fixed or fresh, due to electrode array insertion other than at the site of the cochleostomy [19].

**Intracochlear Trauma.** Several grades of intracochlear traumatization have been described [25]. The least amount of intracochlear trauma seems to be a mild displacement, which appears to be quite common. While it is not known with certainty whether or not this produces damage to neural elements, it is believed that minor displacements of the basilar membrane inward towards the scala

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First report
Adults and children
Synergistic effect of acoustic hearing and electric stimulation
Mean loss of 17.5 dB at 500 Hz
Acoustic sentence and word scores unchanged postoperatively
Conference proceedings, not otherwise published
Near-normal melody recognition
6 patients had enough hearing to provide ITE hearing aid
Long-term data
CNC word scores continued to improve beyond 24 months
27 patients overall
One subject had complete hearing loss after 2 weeks
Pediatric patients
Five European centers
media probably have no adverse effect on auditory function.

Frank perforation of the basilar membrane occurs occasionally and appears to be at least partially related to the stiffness and rigidity of the electrode. However, it appears that perforation of the basilar membrane may occur with any electrode and it may not be possible for the surgeon to prevent this reliably in every case. It appears that injury to the basilar membrane itself will only produce discreet loss of spiral ganglion cells [26, 27]. However, it is hypothesized that if there is mixing of endolymph and perilymph, more widespread loss of hearing can occur [28].

Fraction and dislocation of the osseous spiral lamina have been described as the most severe stage of intracochlear traumatization. Both can be frequently observed with inadequate cochleostomy placement and basal buckling of the electrode once apical resistance is felt. Also, fractures of the osseous spiral lamina are found when the diameter of the electrode is greater than the hosting scala tympani – such as in the apex of the cochlea. The extent to which fracture or dislocation of the osseous spiral lamina produces hearing loss is unclear. Damage to the osseous spiral lamina and basilar membrane in animals appears to produce only discreet loss of those spiral ganglion cells limited to the fractured or torn segments. Widespread loss of ganglion cells is not seen in animals unless damage to the osseous spiral lamina or basilar membrane involves large portions of the cochlea.

**Insertion Technique**

The introduction of the electrode array into the cochlea certainly plays a major part in hearing preservation. Temporal bone studies have shown that deep and forceful insertion procedures can lead to severe destruction of delicate intracochlear structures. However, the authors feel that a 360-degree insertion should be performed to provide good cochlear implant function. The endosteum should be opened by using a gimmick or small Rosen needle. Thereafter, immediate electrode insertion should be performed to prevent loss of perilymph. A small Silastic sheet is placed into the mastoid cavity and through the posterior tympanotomy to prevent contamination of the electrode array with blood or bone dust. The aim during electrode insertion is to slide the array along the outer cochlear wall to its final position. To decrease insertion forces, a drop of surgical lubricant such as hyaluronic acid should be

![Fig. 5. Histological implications on cochleostomy placement. a Taken from a human temporal bone implanted with a MED-EL Standard electrode. A cochleostomy site inferior and slightly anterior to the round window membrane was used resulting in virtually absent intracochlear traumatization. b A histological image of an electrode insertion using a more anterior cochleostomy location. This image demonstrates a fracture of the osseous spiral lamina and disruption of the lateral attachment of the spiral ligament in its inferior portion.](image)
applied onto the opened endosteum. Any forceful procedures should be avoided and the insertion should stop when the point of first resistance is reached. No further insertion maneuvers should be performed afterwards.

**Sealing**

Sealing of the cochleostomy can be achieved via several types of grafts that are placed around the electrode carrier in the cochleostomy region. Up to now, most experience has been with circular or noncircular fascia grafts [6]. Additional fixation with fibrin glue seems to facilitate sealing. Small free muscle grafts are generally used for sealing of the posterior tympanotomy, whereas bone pâté is used to fix the electrode in the mastoid cavity.

**Intra- and Postoperative Adjuvant Medical Management**

The aim of postoperative care is to provide protection against prolonged intracochlear cell death. Intravenous corticosteroids are used to prevent or limit apoptosis of functional cells. Here, several schemes are available. However, dosage should exceed 250 mg prednisolone to guarantee sufficient perilymphatic concentrations. Additionally, intravenous antibiotics help avoid postoperative infection, which could compromise residual cochlear function.

**Discussion**

The extent to which inserting an electrode into the cochlea produces endocochlear damage and injury to neural structures has been a topic of interest since the inception of cochlear implant technology. Even with the application of proper surgical measures, residual hearing is completely lost in at least 10% of attempts. The precise cause of hearing loss in this group of cochlear implant recipients remains obscure and might be multifactorial. We believe that careful assessment of the details of electrode insertional trauma will help eliminate or ameliorate hearing loss in cochlear implant recipients.

Naturally, human temporal bone studies are limited to postmortem examinations. Furthermore, most current electrode arrays used for hybrid patients cause no or very minimal intracochlear trauma if correct surgical principles are employed. Thus, having a foreign body within the scala tympani might be sufficient enough to cause hearing loss. The mechanism for that may involve new tissue formation and compression of the basilar membrane without causing frank trauma. Also, live implantations are performed into unhealthy cochleas demonstrating substantial functional loss. Despite the lack of detailed knowledge of the mechanisms of hearing loss, all those factors should in theory be capable of causing or contributing to it. Therefore, until research has uncovered the exact means, current surgical protocols attempt to implement all possible parameters.

One area that will produce substantial improvements in our understanding of surgically induced hearing loss will be the advent of monitoring methods that can detect real-time changes in auditory function during cochlear implantation. Such technology would allow for direct and live feedback while the electrode is advanced into the cochlea. Hence, the surgeon would be able to stop or retract the electrode once electrophysiologic changes consistent with (early) intracochlear trauma have been observed. This, of course, would require exact characterization of the acute electrophysiologic changes consistent with trauma in both normal-hearing inner ears as well as for various levels of hearing loss. Also, one would have to correlate these electrophysiologic patterns to actual levels of hearing and intracochlear damage. While some attempts of this sort have been made, the utility of these conventional modalities have been limited by reduced signal-to-noise ratios resulting from far-field monitoring among other issues.
Alternatively, it might be possible to directly visualize intracochlear structures during the insertion process. Several technologies might be able to provide this in the near future. However, even those morphologic changes would have to be cross-linked to actual hearing levels and this technology might benefit from its combination with electrophysiologic changes as outlined above.

In summary, ipsilateral hearing preservation in cochlear implantation is possible and clinically feasible. Also, the combination of electric and acoustic hearing has been demonstrated to be beneficial especially for challenging listening environments. With adequate residual hearing, the extra effort seems therefore worthwhile. Current surgical and adjunct medical protocols implement all possible mechanisms of hearing loss until improved knowledge and/or technology can help elucidate the details of intracochlear pathophysiology in response to electrode implantation.

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Minimizing Intracochlear Trauma during Cochlear Implant Surgery


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Electric Acoustic Stimulation in Patients with Postlingual Severe High-Frequency Hearing Loss: Clinical Experience

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Abstract

**Background/Aims:** The aim of this study was to describe audiological outcomes and surgical considerations in electric acoustic stimulation for patients with severe to profound high-frequency hearing loss. **Methods:** In this latest series of patients in our center, all patients were supplied with the new (atraumatic) Flex EAS MED-EL electrode. Eleven patients (age 7.62–71.32 years) with profound high-frequency hearing loss were implanted with this electrode, which was designed to preserve residual hearing despite the intracochlear insertion of an electrode array. All patients were operated on by the same surgeon (W.G.). **Results:** The rate of complete or partial hearing preservation was 100% after a mean follow-up period of 7.85 months (range 0.95–15.65 months). **Conclusion:** This study proves that both refined surgical techniques and atraumatic electrodes are mandatory to preserve residual hearing after cochlear implantation. Flexible, thin, and free-fitting straight electrodes, such as the MED-EL Flex EAS electrode used in this study, seem to most accurately meet the requirements for hearing preservation in electric acoustic stimulation.

Patients with preserved low-frequency hearing and complete hearing loss for high frequencies are mostly unsatisfactorily supplied with conventional hearing aids. Until less than a decade ago, these patients were not seen as possible candidates for cochlear implantation, given the high level of residual hearing and the imminent risk of loss of residual hearing after cochlear implantation.

In 1999, von Ilberg et al. [1] introduced a new treatment modality for this group of patients, the electric acoustic stimulation (EAS). Since then, several studies have proved the superiority of the combined EAS over either modality on its own. These advantages were mainly observed in connection with increased speech recognition in noisy environments, subjective improvements in sound quality when listening to music, and in other situations where the poor frequency resolution and the lack of fine spectral resolution of the electric stimulation on its own have so far proved a disadvantage [2]. In combination with acoustic stimulation, it was possible to observe synergistic effects, presumably because the acoustic hearing assisted in the separation of target voices from
background due to its more precise pitch perception [3].

Several studies have shown that preserving residual low-frequency hearing is a realistic goal for most patients, but until recently there still remained an undeniable number of patients who, despite all efforts, did lose their residual hearing after implantation. Nevertheless, the rate of hearing preservation has steadily increased as a result of our growing experience with more refined and less traumatic surgical techniques and improved electrode designs.

In 1997, Hodges et al. [4] reported a hearing preservation rate of 52% in a series of patients who underwent cochlear implantation with fully implanted standard electrodes. In 2006, Gantz et al. [5] described complete and partial conservation of residual hearing in 46 of 48 patients (96%) using a 10-mm electrode array. Despite this very high rate of hearing preservation, there is evidence for greatly restricted performance in patients who lose residual hearing in the course of time, due to the very shallow insertion depths [6, 7]. In our department, we were able to report hearing preservation in 70% of cases with deep insertion depths (18–24 mm or 360°) [8]. The electrodes used at this time were either standard MED-EL or compressed electrodes with reduced electrode spacing.

In addition to insertion depth, the site of electrode insertion into the cochlea is an important factor for decreasing intracochlear trauma and thereby increasing the rate of hearing preservation. Recent studies have shown that direct round window insertions and round window-related insertion sites are favorable as compared to superior cochleostomies [9, 10]. Finally, if intracochlear trauma is to be reduced, the properties and geometry of the electrode arrays have to be taken into consideration. It was shown that perimodiolar electrode arrays and forceful insertion maneuvers produced greater trauma than atraumatically inserted standard electrodes [11, 12].

In 2004, MED-EL (Innsbruck, Austria) launched a new atraumatic prototype electrode carrier (Flex EAS) in an attempt to minimize the forces generated during insertion and thereby to increase the rate of residual hearing preservation to allow for EAS. An initial temporal bone study [13] confirmed the intended mechanical properties for safe and atraumatic insertion, but clinical results have not been published so far.

In the present study, we evaluated surgical and audiological outcomes achieved with the new MED-EL Flex EAS electrode array. Given the fact that all surgeries were performed by the same surgeon (W.G.) who had already performed many EAS surgeries at the start of this study, learning effects can be largely neglected and the role of the electrode carrier should be clarified in particular.

**Materials and Methods**

**Subjects**
The inclusion criteria for patients were the following: bilateral sensorineural hearing loss with pure-tone thresholds of <60 dB HL in at least two frequencies (125, 250 and 500 Hz) and of >60 dB at frequencies >1 kHz (fig. 1); monosyllabic word recognition ≤40% in the best-aided preoperative condition, and stable hearing loss for at least 2 years prior to surgery. Most patients had symmetric bilateral hearing loss; otherwise, the poorer ear was implanted.

Eleven patients were included in this study (table 1). All patients were implanted by the same surgeon and the study was approved by the local institutional review board. They were supplied with a MED-EL Pulsar cochlear implant with a Flex EAS electrode. The main difference between this electrode and the standard (C40+) electrode is that in the Flex EAS electrode the 5 most apical contacts are not paired, as a result of which the diameter at its tip is oval and reduced to 70% of the standard electrode. Additionally, the electrode spacing is reduced to 1.9 mm (C40+: 2.4 mm), so that the overall distance of electrode distribution is reduced to 20.9 mm (C40+: 26.4 mm). Therefore, when 360-degree insertion depths are used, there is a greater likelihood of all electrode contacts being positioned inside the cochlea than with the standard electrode. For details of this electrode carrier, see Adunka et al. [13].
Fig. 1. Preoperative audiograms for all patients. Bold line represents mean values.

Table 1. Demographic data of all patients

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Sex</th>
<th>Age at surgery, years</th>
<th>Side</th>
<th>Insertion depth, mm</th>
<th>Insertion site</th>
<th>Ossification</th>
<th>Hearing preservation</th>
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<tr>
<td>1</td>
<td>f</td>
<td>60.89</td>
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<td>20</td>
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<td>n</td>
<td>p</td>
</tr>
<tr>
<td>2</td>
<td>f</td>
<td>71.32</td>
<td>left</td>
<td>18</td>
<td>round window</td>
<td>n</td>
<td>c</td>
</tr>
<tr>
<td>3</td>
<td>f</td>
<td>16.15</td>
<td>left</td>
<td>18</td>
<td>round window</td>
<td>n</td>
<td>c</td>
</tr>
<tr>
<td>4</td>
<td>f</td>
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<td>20</td>
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<td>n</td>
<td>p</td>
</tr>
<tr>
<td>5</td>
<td>m</td>
<td>68.20</td>
<td>left</td>
<td>20</td>
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<td>n</td>
<td>c</td>
</tr>
<tr>
<td>6</td>
<td>f</td>
<td>7.62</td>
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<td>22</td>
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<td>n</td>
<td>c</td>
</tr>
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<td>7</td>
<td>f</td>
<td>26.05</td>
<td>right</td>
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<td>p</td>
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<td>p</td>
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<td>right</td>
<td>20</td>
<td>round window</td>
<td>n</td>
<td>c</td>
</tr>
</tbody>
</table>

Promontorium refers to cochleostomy anterior-inferior to the round window. n = No ossification; y = limited ossification; p = partial hearing preservation; c = complete hearing preservation.
Postoperatively, measurements of residual hearing were performed at defined intervals. To provide good performance with the cochlear implant alone, the ipsilateral hearing aid was provided 3 months after the initial fitting of the cochlear implant speech receptor. Residual hearing was assessed at every visit.

Hearing preservation was considered complete when average low-frequency (125–750 Hz) hearing loss was ≤10 dB HL compared to preoperative pure-tone thresholds (table 1; fig. 1–3). Hearing preservation was considered partial in cases of low-frequency hearing loss of more than 10 dB according to preoperative pure-tone thresholds.

To preoperatively test speech understanding, the Freiburg test for monosyllabic words was used at 65 dB with hearing aids in the free-field condition. Sentence understanding was assessed with the Hochmair-Schulz-Moser (HSM) sentence test in quiet and in noise (signal-to-noise ratio of 10 dB). Both tests were performed for each ear separately. Postoperatively, patients were tested with the ipsilateral hearing aid alone, cochlear implant alone, and with the cochlear implant and ipsilateral hearing aid. To eliminate contributions from acoustic hearing when testing the cochlear implant alone, the ipsi- and contralateral ear was closed with an earplug. In all other conditions, only the contralateral ear was blocked.

**Surgical Procedure**

Since EAS surgery is performed on partly functioning inner ears, highest priority is given to perform the procedure with as little trauma as possible (table 2). After a standard mastoidectomy and facial recess approach, the electrode carrier is preferably inserted directly via the round window. The bony niche overhang (subiculum) and the ridge of bone immediately inferior to the round window membrane (crista fenestra, hook region) are removed using slow-rotating diamond drills and skeeters (from stapes surgery). In cases where a good visualization of the whole circumference of the round window is impossible despite a large posterior tympanotomy, a cochleostomy is drilled anterior to the round window. After exposure of the endosteum, the 'EAS fenestra assay' can be tested by carefully touching the stapes. Crystalline steroid solution (triamcinolone, Volon A®) is instilled, and the endosteum (round window membrane) is covered with a drop of hyaluronic acid (Healon) and opened with a fine needle. To minimize the time of inner ear opening, the implant is fixed in its bed before this step. Any suction of perilymph is avoided and the electrode is inserted in an inferior-anterior direction so that it will slide along the inferior and lateral wall of the scala tympani. This direction of insertion was shown to be least traumatic in temporal bone studies.
Table 2. Specific surgical considerations in cochlear implantation for EAS

Preoperative measurement of cochlea length (insertion depth for 360° insertion)

Completion of all drill work before opening of cochlea

Slow rotating diamond/skeeter drill for cochleostomy

Preference of round window insertion

Identification and protection of endosteum, caudal opening with Rosen’s needle

Preservation of perilymph

Intracochlear and systemic application of corticosteroids

Application of hyaluronic acid (Healon) to ease electrode insertion

Slow insertion of electrode (allow outflow of perilymph), in inferior-anterior direction (sliding against lateral wall of scala tympani)

Fig. 3. Difference between pre- and postoperative thresholds for individual subjects and mean values at the end of the study (bold line).
To minimize intrascalar pressure waves and to allow a compensational outflow of perilymphatic fluid, the electrode insertion is carried out slowly, over a period of approximately 3 min. With the electrode carrier in place, the cochleostomy is sealed with a circular fascial flap.

A 360-degree insertion of the electrode was aimed for in all procedures. To compensate for variations in cochlear size and diameter, a computer tomography-based measurement of the cochlea was performed preoperatively [15]. The insertion depths to achieve a 360-degree insertion were then estimated by the radiologist and carried out by the surgeon. In our experience, a 360-degree insertion of the array (corresponding to 18–22 mm in this study) calculated to enter the 1,000-Hz region, which defines the end of electric and beginning of acoustic stimulation, is sufficiently deep to guarantee satisfying performance combined with acoustic stimulation, as well as with the cochlear implant alone in case of loss of residual hearing.

Results

A total number of 11 patients (8 females, 3 males; mean age at implantation 48.36 years, range 7.62–71.32 years) with significant residual hearing according to our protocol were implanted between 2004 and 2008 and could be included in this evaluation (table 1). The mean follow-up time was 7.85 months after implantation (range 0.98–15.65 months).

In 3 patients (No. 8, 9, 10), there was limited ossification at the site of cochleostomy (round window), but otherwise surgery was uneventful in all cases. Electrodes were inserted at a depth of 18–22 mm, corresponding to 360°, as determined by the preoperative radiological assessment and confirmed by the postoperative X-ray.

Patients were grouped according to their individual hearing preservation outcome at the end of the study (table 1). Of the 11 patients, 5 (45.4%; fig. 2, 3) showed complete hearing preservation under the terms of our protocol (see above). In 6 patients (54.5%), it was possible to partially preserve residual low-frequency hearing. There was no complete loss of residual hearing at the end of this trial.

Mean monosyllabic test scores improved after a mean follow-up period of 7.85 months from 9% correct with the hearing aid alone to 48% with the cochlear implant and to 65% in the EAS mode. Mean values of HSM sentences in quiet increased from 30% in the hearing aid alone condition to 75% in the cochlear implant condition and to 79% in the EAS condition. HSM sentences with a 10-dB signal-to-noise ratio increased from 10% in the hearing aid alone condition to 42% in the cochlear implant alone condition and to 50% in the EAS condition.

Discussion

In this study, all patients were supplied with the new MED-EL Flex EAS electrode and complete or partial hearing preservation was accomplished in all 11 patients. Five of the 11 patients achieved complete and 6 patients partial preservation after a follow-up period between 0.98 and 15.65 months. To our knowledge, these data represent the highest rate of hearing preservation despite deep (360°) electrode insertion.

In a recent publication, we reported a 70% rate of complete and partial hearing preservation with standard electrodes [8]. Given the fact that the implanting surgeon had already performed several hundred cochlear implantations at the beginning of this study, learning effects can be widely neglected for the outstanding results. Indeed, the diameter and flexibility of the electrode carrier seem to play a crucial role to reduce intracochlear trauma. Nevertheless, specific surgical considerations have been refined in our center to preserve residual hearing with the highest likeliness (table 2).

Several factors seem to be responsible for a preservation or loss of residual hearing. Among these factors, the question of how deep electrode arrays should be inserted in EAS patients is still a controversial one. Temporal bone studies have shown that deep insertions increase the degree of intracochlear trauma and tissue reaction, and
therefore significantly contribute to the success or failure of intraoperative hearing preservation [16, 17]. Based on these findings, Gantz and Turner [18] introduced a 10-mm electrode array with 6 active contacts (Nucleus Hybrid CI) and Gantz et al. [5] were recently able to report complete hearing preservation (within 10 dB of preoperative thresholds) in 52% of the patients and complete or partial hearing preservation in 46 of 48 patients (95.8%).

Nevertheless, several studies have described the importance of the apical cochlear region for speech performance [19, 20]. Therefore, even if very shallow insertions seem better suited to achieving residual hearing preservation, poor performance with electric stimulation alone was observed in cases of loss of residual hearing [6] and in patients with mid-frequency hearing loss [21]. Some authors recommend shallow implantations and full-length reimplantation in cases of loss of residual hearing [6]. We believe that a minimum insertion of the electrode array of 360° is necessary to guarantee satisfying performance with the implant alone even in case of loss of residual hearing [7]. A radiological method was therefore developed to preoperatively predict the required insertion depth to achieve a 360° insertion [15].

Another important factor for the minimization of intracochlear trauma is the site of electrode insertion. Trauma to cochlear structures may lead to unwanted degeneration of neurons through the activation of enzymatic cascades, the release of neurotoxic factors, and subsequent tissue reaction. In temporal bone studies, several authors found round window insertions being less traumatic than conventional cochleostomy approaches. Direct round window insertions limit the amount of drilling and thus reduce the risk of acoustic and mechanical trauma to the inner ear [22, 23].

The results of our study seem to support this assumption: all patients with complete hearing preservation underwent direct round window insertions. In patients with ossification around the round window (patients No. 8, 9, 10), which necessitated more extensive drilling, hearing could not be preserved completely.

In addition to investigating sophisticated surgical techniques, such as avoiding bone drilling after incision of the endosteum, slow electrode insertions in inferior-anterior directions, and application of intrascalar glucocorticosteroids (table 2), this study aimed to answer the question as to how far the geometrical properties of electrodes influence the preservation of residual hearing in EAS surgery. The fact that the Flex EAS electrode features only single stimulation contacts in the apical region results in a reduced number of metal wires within the silicone body, in smaller cross-sectional dimensions, and hence in a higher flexibility especially in the tip region. In temporal bone studies, Adunka et al. [13] demonstrated a reduction of insertion forces of more than 40% as compared to standard electrodes.

The clinical results presented in this series of patients confirm the histological findings. So far, highest hearing preservation rates with electrodes inserted at similar insertion depths ranged between 70 and 90% [8, 24], even reaching 100% in this study. Using 10-mm inserted electrodes, Gantz et al. [5] described hearing preservation rates of up to 96%. On account of the foreseeable shortcomings of such shallow insertion depths, Lenarz et al. [21] considered 10-mm insertions not adequate and introduced a similar, slightly longer electrode (Hybrid-L), which is inserted up to 16 mm. According to temporal bone studies [11, 12], perimodiolar electrodes produce a higher degree of intracochlear trauma than free-fitting electrodes. Recently, however, clinical evidence for atraumatic perimodiolar implantations with preservation of residual hearing has been described. In a multicenter study, Garcia-Ibanez et al. [25] found preservation of residual hearing in 71–86% of subjects after implanting the Nucleus Contour Advance electrode. Nevertheless, due to the very low degree of preoperative residual hearing, postoperative measurements are difficult to
differentiate from vibrotactile impressions and results can therefore not be directly compared to our results.

**Conclusion**

Performing EAS surgeries since the very beginning of this technique in 1999, in the series of patients presented herein, we could achieve hearing preservation in all patients for the first time. If certain surgical aspects and limited insertion depths are respected, slim, free-fitting, and flexible electrodes, such as the MED-EL Flex EAS electrode used in this study, seem to be of crucial importance for a reliable preservation of residual hearing.

**References**


The Hybrid Cochlear Implant: A Review

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Abstract

The Hybrid S or ‘short-electrode’ cochlear implant was developed to treat patients with a severe to profound hearing loss limited to the high frequencies. The short electrode is implanted into just the base or high-frequency region of the cochlea, with the goal of preserving residual low-frequency hearing. As a result, electric stimulation can be combined with acoustic stimulation in the same ear (and the opposite ear); this is one instance of ‘acoustic plus electric’ (A + E) stimulation. In this paper, we will review the latest findings from the first two stages of the clinical trial for the Hybrid concept in the United States. Generally, we will review surgical techniques, clinical trial criteria, residual hearing preservation, improvements in speech perception in quiet, and predictive factors for patient benefit. We will also discuss the significant benefit of A + E stimulation for speech perception in noise and musical measures of melody and instrument recognition, as well as valuable insights into central auditory nervous system plasticity gained from the use of a very short electrode array.

Background

In most cases of mild, moderate, or even severe hearing loss (HL), the auditory receptors are damaged, but hearing aids (HAs) can still provide enough amplification for individuals to understand speech. However, for cases of severe to profound HL, HAs often fail to provide improvement in speech recognition [1, 2].

Cochlear implantation is now a well-established and efficacious means of restoring verbal communication skills to postlingually deafened adults with severe to profound HL. They are among the most successful neural prostheses, with improved speech recognition in quiet for the majority of cochlear implant recipients; however, speech recognition in noise and enjoyment of music has remained poor.

One overlooked segment of the hearing-impaired population is individuals with a steeply sloping high-frequency (HF) HL, which is a common pattern of adult sensorineural HL. The pattern of relative preservation of low-frequency (LF) hearing with a down-sloping progressive HF HL may be seen in familial HL, presbycusis, ototoxicity, and noise-induced HL. Patients lose word understanding because consonants are heard in the HFs. These patients do not benefit fully from amplification because of the severity of the HF HL [3], but do not qualify for a standard cochlear implant because of the usable residual LF hearing. Since cochlear implants are typically implanted fully into the cochlea, the implantation process often destroys remaining
auditory structures and thus the residual acoustic hearing.

The development of the Hybrid S, or ‘short-electrode’ cochlear implant, began in 1996 at the University of Iowa in cooperation with Cochlear Corporation to specifically treat this patient population [4, 5]. An FDA feasibility clinical trial with the Hybrid S implant was initiated in 1999. Instead of a full-length cochlear implant, a shorter version is implanted into the basal cochlea, using ‘soft surgery’ techniques to preserve the architecture of the apical cochlea. As a result, the residual apical structures and associated LF hearing can be preserved. This allows for a bimodal mode of listening: LF information provided acoustically via an HA, and HF information provided electrically through the implant. The Hybrid device is thus one implementation of the concept of ‘acoustic plus electric’ (A + E) stimulation, in which the acoustic and electric components are provided to the same ear. A + E strategies are also being employed in Europe, with a modified technique but standard electrode length [6–9]. In this paper, we will limit our scope to reviewing the latest findings from the first two stages of the clinical trial for the Hybrid S device in the United States.

The initial questions asked were: (1) Can residual hair cell function for acoustic hearing be preserved following implantation of the ‘short’ cochlear implant? (2) Can patients successfully integrate acoustically and electrically transmitted speech cues for improved speech recognition? This paper presents the results of the Iowa/Nucleus Hybrid Implant phase I and II clinical trials, and reviews our expanding appreciation of the benefits and limitations of electroacoustic processing as well as the plasticity of our auditory system.

Methods

Overview of the Hybrid Clinical Trial

In the initial feasibility study, patients were implanted with two versions of a cochlear implant based on the Nucleus CI24 implant (Cochlear Corporation). The first design consisted of a 6 × 0.2 × 0.4 mm electrode with 6 channels. The second design increased the length of the electrode to 10 mm with the active electrodes at the distal 6 mm.

The initial single-site feasibility study was then followed by a multicenter FDA-controlled clinical trial. Based on the initial data, the 10-mm device was selected for the clinical trial. For phase I, the study was expanded to 9 investigational sites and 25 more subjects were implanted with the 10-mm, Nucleus 24-based receiver and stimulator (CI24M). For phase II, the study was expanded to a total of 16 sites and 58 subjects were implanted with the same 10-mm array, but paired instead with a Nucleus Freedom-based receiver and stimulator (CI24RE) (Hybrid S8).

Subjects

Patients receiving the Hybrid cochlear implantation were postlingually deafened adults with <60 dB HL below 500 Hz and >80 dB HL above 2,000 Hz. The specific required hearing profile is shown in figure 1 (light-gray for phase I; dark-gray for expanded profile range under phase II). Additional inclusion criteria in phase I were consonant-nucleus-consonant (CNC) monosyllabic word recognition scores of 10–50% in the worse-hearing ear and <60% in the better-hearing ear. In phase II, these criteria were broadened to 10–60% in the worse ear and <80% in the better ear.

Preoperative audiometric evaluation included pure tone audiometry and CNC scores. Daily bilateral HA use was a prerequisite for implantation. At initial evaluation, HA checks, or fittings if the patient had not previously used amplification, were performed to ensure optimal fit. All patients underwent at least 2 weeks of optimally fitted daily bilateral HA use prior to establishing preoperative speech discrimination scores, as well as implantation.

Surgical Technique

Our surgical technique of soft insertion has been detailed in multiple publications [10, 11]. The most important tenets are given below.

(1) Completion of exposure, bony work, and soft tissue work before completing the cochleostomy. This includes drilling the well for the electronic package, harvesting and constructing a temporal fascia washer. The facial recess or posterior tympanotomy must be opened to allow complete visualization of the round window. The overhanging niche of the round window must be removed using a diamond burr completely exposing the entire round window membrane. These steps minimize the open cochlea’s exposure to blood and bone dust.

(2) Minimally traumatic cochleostomy. A strategy similar to that used to perform a ‘drill-out’ stapedectomy...
should be employed. The cochleostomy must be placed approximately 1 mm anterior and inferior to the floor attachment of the round window membrane. The promontory of the cochlea in this portion can be more than 1 mm thick. It is suggested that the promontory be saucerized in this region with a 1-mm diamond burr. Placement of the cochleostomy in the anterior-inferior position to the round window membrane avoids damage to the scala media and spiral ligament. The burr should not enter the scala tympani. The endosteum is opened with a 0.2-mm footplate hook. The smallest cochleostomy needed to insert the implant is made (0.5–0.7 mm). No suctioning of perilymph is permitted.

(3) Minimally traumatic insertion. Short lapse of time between opening the cochlea and insertion is emphasized. The electrode is stabilized with a suture at the lateral tegmen mastoid cortex prior to insertion into the cochlea. Actual insertion of the electrode is slow (30–45 s) to minimize intracochlear trauma.

**Programming of Processor and Hearing Aid**

All patients’ processors were programmed with a standard ACE strategy (with 6 of 6 peaks, so essentially CIS).

During the initial feasibility study, each patient was provided with a range of MAP frequency allocations to wear every day and so empirically chose their preferred frequency allocation. During the multicenter clinical trial (phases I and II), each patient was provided with a single default MAP frequency allocation that was selected to complement the frequencies available from that patient’s residual hearing. Since patients eligible for the study typically had a residual hearing cutoff around 1,000 Hz, typical MAP frequency allocations would be either 688–7,938 or 1,063–7,938 Hz.

Patients in the initial feasibility study and phase I of the clinical trial used either the SPRINT, SPEAR, or ESPRIT processors, but eventually upgraded to the Freedom processor by the current date. Patients in the second stage of the trial were provided with the Freedom processor at initial activation.

Most, but not all, patients wore HAs in both the implanted ear and nonimplant ear. Typically, the HAs in both ears were programmed to complement the frequency range provided by the implant, with a high-pass cutoff matching the low-pass cutoff of the implant frequency allocation range. A few subjects did not use one or both HAs either because they had near-normal LF hearing, or because they had very little residual hearing and relied on the implant alone.
Approval and Institutional Review
The University of Iowa Human Subjects Investigational Review Board approved the Hybrid electrode investigation. Likewise, the individual institutional Investigational Review Boards at each of the participating implantation centers approved the investigation at each phase of the study. The FDA approved the Iowa/Cochlear Hybrid Implant for a phase II multicenter trial. The Hybrid S8 investigation was conducted under FDA feasibility IDE No. G990155.

Results

The initial feasibility study included 3 patients at the University of Iowa implanted with the original 6-mm Hybrid electrode, and 4 patients implanted with the 10-mm Hybrid S8 (S8). The multicenter phase I included 25 subjects implanted with the S8. Fifty-eight subjects at multiple institutions were implanted with the S8. A total of 87 patients received the 10-mm S8 electrode. There were 11 phase II withdrawals prior to completion of the study. Fourteen patients were reimplanted with a standard-length electrode (n = 2 from the initial 6-mm feasibility trial, and n = 12 from phase I/II). Three patients received a contralateral standard electrode after Hybrid implantation due to progressive sensorineural HL in the contralateral ear.

Hearing Preservation
The overall residual hearing preservation results for the multicenter study are shown in figure 2a and b. Overall, 79/87 (91%) patients had good preservation of residual hearing, performing within 30 dB of their preoperative LF (125–750 Hz) thresholds (LFT) at initial activation (fig. 2a). The mean LFT shift was 14.6 dB at 1 month after surgery, and 41/87 (47%) had average LFT within 10 dB of baseline. Two patients (2%) experienced total HL within 1 month of surgery. Some patients experienced a delayed increase in their sensorineural HL. Sixty-one of 81 (75%) subjects maintained LFT within 30 dB of their preoperative pure tone average by the end of the trial (fig. 2b; 1–5 years after activation for all included patients).
The total number of patients losing all residual hearing is 8/81 (10%).

**Speech Recognition in Quiet**

Gantz and Turner [4, 5] reported the results from the initial single-site feasibility study begun in 1999 at the University of Iowa. A variety of MAPs were provided to the subjects, and the most successful MAPs were those that presented speech from 1,000 to 8,000 Hz, or from 2,000 to 8,000 Hz. In all subjects, comparison of preoperative and postoperative acoustic-only scores showed that speech recognition with the acoustic hearing was preserved after implantation, along with the residual hearing.

Larger performance improvements were seen for patients with the 10-mm array than for patients with the 6-mm array. Subjects with the 6-mm array showed on average only a 10% improvement in consonant recognition scores under the Hybrid condition (implant plus HA in the implant ear). In contrast, subjects with the 10-mm array showed an average of 40% improvement in consonant recognition scores. The 10-mm subjects also showed larger improvements in understanding of monosyllabic words (preoperatively ranging from 20 to 43% and postoperatively ranging from 83 to 90%) and sentence recognition (100% postoperatively) under both the combined (implant plus HA in both ears) and the Hybrid conditions. The greater success of the 10-mm over the 6-mm array may be explained by the larger tonotopic mismatch for the 6-mm array, as a similar effect was seen in simulations of cochlear implant listening with various amounts of tonotopic mismatch [4]. Alternatively, the 6-mm array may not extend deeply enough into the cochlea to successfully stimulate surviving nerve fibers or spiral ganglion neurons.

Also noted in this initial study was the strong effect of duration of implant experience on the A + E benefit; all 4 patients with the 10-mm array took at least 10 months to fully adapt to the Hybrid device and maximize their speech recognition benefit.

Gantz et al. [11] described the speech perception results for 19 subjects, mostly from phase I, who had at least 9 months of experience with the 10-mm array. Fifteen of 19 subjects demonstrated a significant benefit in monosyllabic word recognition under the combined condition postoperatively compared to the bilateral HA condition preoperatively. One interesting observation was that 2 of the 4 individuals that did not show significant benefit had long durations of HF HL (>40 years). The effect of implant experience was strong again in this larger subject pool, with substantial improvements often seen between 3 and 12 months, and between 12 and 24 months for some subjects.

Reiss et al. [12] showed that some individuals, when tested on consonant recognition, performed surprisingly well with just the electric (implant) stimulation (E-only), i.e. without any added acoustic information. In fact, Hybrid patients as a group performed as well as long-electrode users when tested on consonant discrimination under E-only conditions.

More recent results from Gantz et al. [13] indicate that the majority of subjects implanted in the multicenter clinical trial to date have benefited from the device. Out of a total of 87 subjects, 61 subjects with 9–12 months of experience had been tested on CNC word recognition and BKB_SIN tests. Improvement in either word score or speech reception threshold was observed in 45/61 (74%). Improvement in both scores was observed in 29/61 (48%). However, 14/61 (23%) subjects had either no improvement or significantly diminished performance on both CNC word recognition and speech reception threshold tests after 9–12 months of use as compared to their preoperative baseline; therefore, it is important to isolate the relevant preoperative factors that determine whether a patient will benefit from a Hybrid device (described in the next section).

It should be noted that there was no correlation of benefit with the amount of residual hearing remaining in the implant ear; this may be due
in part to the ability of some Hybrid patients to obtain significant benefit from electric stimulation alone.

**Predictive Factors for Success**
A variety of potential predictors were subject to a multiple regression analysis via AIC model selection [13]. Preoperative CNC scores ($\beta = 0.52$, $p < 0.01$) and duration of deafness ($\beta = -0.46$, $p < 0.02$) were both shown to be significant predictors of postimplantation performance. A model considering all implanted subjects that included both of these variables explained 23% of variance ($R^2$). This was the best-fit model, compared with other predictor variables such as age at implantation or age at onset of deafness. When the poor performers ($n = 14$) were considered separately from good performers ($n = 45$), 91% of the variance in performance was attributable to preoperative CNC scores plus duration of deafness.

**Speech Recognition in Background Talkers**
Turner et al. [14] also showed results for recognition of spondee words (2-syllable words) in the presence of two background talkers. The level of the target words was held constant and background was varied adaptively to find the signal-to-noise ratio (SNR) eliciting 50% correct performance. A lower SNR is a better score because it means that the patient can understand speech in more adverse noise conditions. Note that the use of two-syllable words makes this test an easier test than most tests of speech recognition in noise; therefore, it specifically measures the ability to resist the detrimental effects of background noise without depending on speech recognition abilities for more difficult sounds in quiet.

This test was conducted in normal-hearing, hearing-impaired, long-electrode, and Hybrid subjects tested at Iowa; the group results are compared in figure 3. The normal-hearing subjects performed the best at the lowest SNRs, followed by hearing-impaired subjects (grouped by severity of HL), and the Hybrid patients. Long-electrode patients performed the worst, with an average positive SNR required to understand the spondee words. The Hybrid group had a significant advantage over the long-electrode group of 4–5 dB on average [11, 13, 15]. However, it should be noted that some individual Hybrid subjects were able to perform the task at 15–20 dB lower SNRs than the best long-electrode subjects, and thus showing the impressive potential benefits of preserving residual acoustic hearing.

These results point to the acoustic hearing as the main contribution to this advantage. When performance levels were compared within subjects under E-only, Hybrid, combined, and A-only conditions, performance was generally similar for all conditions utilizing acoustic hearing, but much worse for the E-only condition. Further, the benefit of acoustic hearing was seen regardless of whether the acoustic hearing was from the implant or nonimplant ear [16, 17; Reiss et al., unpublished].

The benefit of acoustic hearing does not seem to be correlated with the degree of HL, up to severe levels, as long as the hearing is aided [15, 16]. In cases of profound or near-total HL after implantation with the Hybrid, the benefit is lost, most likely because A + E stimulation in these cases is really E-only stimulation [13].

**Music Perception**
Hybrid subjects were also compared with normal-hearing listeners and long-electrode subjects on the recognition of familiar musical melodies as well as recognition of musical instruments [18]. Familiar melody recognition was tested under two conditions: melodies with sung lyrics and melodies played by instruments without lyrics. With lyrics, the Hybrid group showed no significant difference in melody recognition scores from the normal-hearing group with average scores around 70%, and performed significantly better than the long-electrode group (average scores around 30%). Without lyrics, all three groups were significantly different, with the normal-hearing
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group performing the best, the Hybrid group performing in between, and the long-electrode group performing the worst. It is likely that the recognition of melodies without lyrics was assisted by the availability of preserved LF pitch information, information that is not transmitted through conventional signal processing. On the test of instrument recognition, accuracy depended on the frequency range of the instruments being played, as the Hybrids were significantly worse than the normal-hearing group only for the medium and HF categories, and not for the LF category. These two test results suggest that the preserved LF residual hearing made an important contribution for these two musical tasks of melody recognition and musical instrument recognition in the Hybrid group.

Pitch Perception

Previous experiments on pitch perception through a cochlear implant have found pitch estimates to be lower than predicted based on the cochlear location of the electrodes [19, 20]. Recent work with Hybrid patients has suggested a compelling possible explanation for this discrepancy [12, 21]. In these patients, the electric pitch perceived through a single electrode in the Hybrid device was measured by comparison with an objective reference: the acoustic pitch perception in the nonimplanted ear. These pitch measurements were followed in each subject over time, that is, at various times from hookup to as long as 5 years of implant use.

This study led to a surprising finding: the pitch perception changed with implant experience in several subjects, in some cases by more than 2 octaves. The pitch could become higher, lower, or oscillate over time, but generally the trend was for high pitches to drop, low pitches to rise, and pitches in an intermediate range to remain the same. Initial data suggest that the pattern of changes may be determined in part by the severe tonotopic mismatch between the original sound frequencies and the cochlear place of stimulation introduced by the speech processor MAP, and the changes in perceived pitch may in fact be driven by this tonotopic mismatch [12].

Fig. 3. Comparison of speech in noise for Hybrid patients, long-electrode patients, hearing-impaired patients, and normal-hearing subjects. The values shown are SNRs (in dB) for 50% correct recognition of spondee words in competing backgrounds of steady noise (black bars) or competing talkers (white bars). Subjects are sorted according to degree of hearing loss (average of 500, 1,000, and 2,000 Hz) and also if they are listening through a traditional long-electrode cochlear implant or Hybrid cochlear implant. Figure reprinted with permission by Gantz et al. [11].
Specifically, for the Hybrid device, the theoretical cochlear place of stimulation for the 6 Hybrid electrodes should be in the range of 4,000–9,000 Hz, even if the possibility of stimulation of nerve at the spiral ganglion instead of at the organ of Corti is accounted for [22, 23]. Compare this to the typical speech processor allocation of environmental sounds from 688 to 7,938 or from 1,063 to 7,938 Hz. This is a consequence of the standard practice of programming MAPs to provide the sound frequencies that the patient is missing, regardless of the cochlear place-frequencies that are actually stimulated by the implant. However, despite the severe tonotopic mismatch, there was no significant difference in speech recognition scores between a mismatched and matched allocation [15]. Presumably, the loss of usable LF and mid-frequency speech information with a more normal HF allocation balances out any advantage of more closely matching sound frequency to cochlear place of stimulation. This is reflected in the patients’ preferences for the broader MAP despite the tonotopic mismatch that is introduced. In the words of one patient, a matched 3,000- to 8,000-Hz MAP was ‘great for listening to bird calls but that was about it’ [pers. commun.].

Conclusions

The clinical trial results have shown that (1) residual hearing can be preserved with a short-electrode cochlear implant and soft surgery approach to implantation, and (2) Hybrid patients do very well with combined A + E stimulation – comparable to long-electrode patients in quiet, and often better in background noise and in musical tasks such as melody and musical instrument recognition that require more refined spectral information.

Overall, many patients who have received the Hybrid cochlear implant report high satisfaction with the device [unpubl. obs.]. This study has shown a clear benefit of A + E hearing over E-only hearing for speech in noise and music appreciation. Further, the benefit of the residual acoustic hearing does not depend strongly on the amount of residual hearing preserved [15]. Residual acoustic hearing has also been shown to aid speech recognition with the implant in noise even when it is useless for speech recognition in a quiet, A-only hearing setting [24].

In addition, some unexpectedly valuable insights have been gained from the use of a short-electrode implant. First, patients are readily able to adapt to a severe tonotopic mismatch of speech processor frequency information to the cochlear place of stimulation, in contrast to early studies that suggested that correct allocation of place-frequency information was important for speech understanding [25, 26]. These results suggest that experience with tonotopic mismatch is important for giving patients time to adapt, consistent with more recent studies [27, 28].

Second, Hybrid patients still perform very well with E-only hearing, even if residual hearing is lost. This is surprising, considering that there are only 6 electrodes in a very narrow region of the cochlear base. Implantation of the full length of the cochlea therefore may not be necessary for full benefit (even for long-electrode patients) given our subjects’ ability to adapt to tonotopic mismatches over time.

Third, the Hybrid device, with the introduction of a very large tonotopic mismatch, has demonstrated that cochlear implant pitch perception can change with experience. In fact, the large tonotopic mismatch may drive the pitch changes. This finding implies that peripheral attributes, such as nerve survival or electrode position, do not completely account for pitch perception. Pitch perception is plastic and may be adaptable with experience. This may not be as applicable to older patients, however, as they seem less able to adapt to the Hybrid device. Central plasticity and the ability to adapt to tonotopic mismatch may depend on age, as well as duration of deafness.
There are other potential advantages of preserving residual hearing in both the implant and nonimplant ears that have not yet been studied; these include the availability of binaural acoustic inputs for spatial localization and speech recognition in the presence of background talkers from multiple locations. Therefore, surgeons should consider attempting to preserve residual hearing in all cochlear implantations, including long-electrode devices, regardless of the amount of residual hearing preserved.

Finally, even though the Hybrid device can be considered a success in the majority of patients, a consistent 10% of patients eventually lost all residual hearing. This rate of HL occurred at different points along the clinical trial, suggesting that this adverse effect is not an issue of a learning curve in the device insertion. The finding that the implant did not negatively impact initial A-only speech recognition suggests that the presence of the electrode array in the cochlea did not alter residual inner hair cell function or interfere with the biomechanics of the apical organ of Corti [4, 5]. However, the postoperative HL is asymmetric with the natural progressive sensorineural HL in the contralateral ear and thus is likely stemming from the surgery or the device itself. It is unclear why this happens, why loss of residual hearing also has a subacute or even fluctuant course, or if there are any common elements between those subjects who lost their hearing. The problem of delayed HL after initial preservation needs to be studied further.

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References


Electric Acoustic Stimulation in Children

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Abstract

Background/Aims: The combined electric acoustic stimulation (EAS) of one ear is a topic that has received considerable attention over the last 10 years, the technique having originally been introduced by Prof. Christoph A. von Ilberg for so-called borderline adult cochlear implant (CI) candidates. Its development has followed several parallel strands, including the modification of existing surgical approaches and the use of different CI devices (including new designs of electrode), as well as having been applied to various different groups of patients. The aim of the study described herein was to investigate the application of EAS in children with partial deafness (PD).

Methods: In 2002, we performed the first implantation of an adult patient with PD, in which we pioneered the technique of partial deafness cochlear implantation (PDCI). Encouraged by the outstanding results achieved by the application of EAS in adults, we have extended its application to children who have a significant amount of residual hearing in the ear selected for implantation. Between September 2004 and December 2007, 15 children with PD and 10 platinum hearing aid users were implanted with either a COMBI 40+ or a PULSAR, using the ‘round window’ technique to increase the probability of hearing preservation.

Results: Monosyllabic word recognition increased over a 12-month period in the platinum group, from 31 to 60% under quiet conditions and from 1 to 19% under noisy conditions. In the PDCI group, the commensurate increase was from 34 to 67% under quiet conditions and from 7 to 47% under noisy conditions.

Conclusion: The application of EAS in children gives them the ability to understand speech, hence allowing the child’s overall communication skills to be improved by increasing their efficiency and effectiveness.

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of competing sounds, can reduce the opportunities for incidental learning through overhearing, which are known to play a significant role in child development.

The perception and interpretation of the suprasegmental features of speech, such as intonation, stress, and emphasis, can be significantly impaired in children with CIs (mainly due to limitation c above). Furthermore, Most and Peled [4] found that children with CIs perform significantly less well in stress and intonation tests than children with profound hearing loss who used HAs. Because suprasegmental features are essential for communication, restricted access to them can adversely affect the (re)habilitation process in children with CIs.

In addition, the musical appreciation of children with CIs is poor (mainly due to limitation b above), and this phenomenon can offset the possible advantages of musical training [5]. Musicality and music training in children may have a positive effect on language, cognition, and social development in children. In order to realize the aim of pediatric cochlear implantation by increasing access to speech information, continued efforts must be made to overcome the limitations of CI systems. One possible approach is the application of electric acoustic stimulation (EAS).

**Possible Advantages of Electric Acoustic Stimulation in Children**

The combined EAS of one ear was first proposed by von Ilberg et al. [6] and later achieved in adults using an HA and a CI in the same ear [7–9] or via the use of natural nonamplified low-frequency hearing and CIs in a group of patients with partial deafness (PD) [10–12]. There are also reports of benefits from EAS that accrued from the application of DUET™ processor, which combines speech processor and HA in one device [13, 14]. EAS in children can make up for the limitations of CI systems (see limitations a–c above) on the basis of the same mechanisms that underlie the benefits of combined EAS in adults.

By summarizing the detailed discussion of the possible mechanisms involved in EAS presented by Turner et al. [15], Qin and Oxenham [16], and Dorman et al. [17], the following advantages of using EAS in children are apparent:

1. Acoustic stimulation of the apical region can improve frequency resolution at low frequencies (thus compensating for limitation a above);
2. Using EAS, fine structure information is presented without modification in the low-frequency range (thus compensating for limitation b above), and
3. This fine structure information is likely to include F₀ (thus compensating for limitation c above).

On the basis of the significant body of evidence of the benefits of EAS observed in adults, we believe that the application of EAS in children can considerably enhance their auditory and linguistic experiences and facilitate cognitive and linguistic functioning, thus enabling the child to follow more closely a normal course of development. The use of EAS in children of course requires the implantation of a child with residual hearing, and the preservation of this residual hearing during the surgery. The use of CIs in children with residual hearing is not entirely new because of the changes in the criteria of qualification for this procedure over the last 20 years.

**Cochlear Implantation in Children with Residual Hearing**

It is generally accepted that CIs may be offered to children who have little potential for speech understanding, due to the limited benefits of acoustic stimulation using a well-fitted HA, although the definition of ‘limited benefits’ has been altered many times over the last 20 years. Originally, only those children who had very little residual hearing and who showed no demonstration of sound
awareness using HAs were considered to be candidates for cochlear implantation. By assuming a relationship between the degree of residual hearing and the benefit conferred by the use of an HA, a classification of children with sensorineural hearing loss from ‘good’ to ‘poor’ HA user was then proposed, based on pure tone average (PTA), using the scale bronze (for PTA >110 dB), silver (for 110 > PT A > 100 dB), and gold (for 100 > PTA > 90 dB) [18]. Gradually, the criteria for implantation have been expanded to include children with better residual hearing, and now include silver and gold HA users. This change in the criteria of qualification was supported by the observation that implanted children in all three classes performed better than their peers who used HAs and had comparable hearing loss. More recently, a platinum HA user group was defined for PTA between 60 and 90 dB [19]. It was shown that hearing in implanted children in the platinum group was better with a CI than with an HA.

Several researchers have reported that children who have some degree of residual hearing before implantation achieved better speech perception skills than those with poorer hearing [20–22]. A degree of residual hearing before implantation can therefore be conducive to successful implantation.

Preservation of Hearing after Cochlear Implantation

Children with Residual Hearing
The opinion that preservation of any residual hearing must be an aim of all CI surgeries has recently been expressed by authors reporting on the use of EAS in adults [7, 8]. The result of relaxing the qualification criteria that allow increasing numbers of children with residual hearing to be implanted has been to ensure that the preservation of their residual hearing should be taken into consideration. Although the preservation of hearing in adults has been extensively reported [23–25], publications on this issue in the pediatric literature are few and far between. Skarzynski et al. [26] assessed hearing preservation in 7 children and 19 adults implanted with the COMBI 40+ system and found that only 19% of patients lost all measurable hearing after cochlear implantation. Interestingly, variables such as age and duration of deafness did not influence the preservation of residual hearing in their study. In contrast, Kiefer et al. [27] proposed that children are more likely to retain their residual hearing than adults.

Willingham and Manolidis [28] compared postoperative auditory steady-state response (ASSR) thresholds to preimplant thresholds in a group of 12 children implanted with the MED-EL COMBI 40+ system. There were no statistically significant differences between the pre- and postimplant ASSR thresholds at 250 and 500 Hz, and at 1, 2, 4 and 8 kHz in the implanted ear. The results of their study showed that it is possible to preserve residual hearing in children at a level that is at least no worse than in adults. In order to combine acoustic and electric hearing (using EAS), a sufficiency of residual hearing is required at low frequencies. However, it is still unclear how much residual hearing is sufficient for effective EAS. In studies of combined EAS in adults, James et al. [29, 30] and Frayesse et al. [31] proposed that the criteria for inclusion in conventional candidates for cochlear implantation should be postoperative thresholds of 80 dB (for 125 and 250 Hz) and 90 dB (for 500 Hz), in order that residual hearing could be achieved with a high-power HA. By applying these criteria to children, it may be assumed that those children who are platinum HA users usually possess enough residual hearing to be considered as EAS candidates.

Children with Partial Deafness
In a recent study, a new group of children with PD, who fell outside of the typical selection criteria, was identified as being potential candidates for EAS. Skarzynski et al. [10] describe PD as being characterized by normal or slightly elevated thresholds at
low frequencies with almost total deafness at higher frequencies. Children in this group remain beyond the scope of effective treatment using HAs alone. Such children had not previously been considered for cochlear implantation, because it was feared that this intervention would damage the functioning part of the cochlea. Encouraged by the outstanding results achieved following partial deafness cochlear implantation (PDCI) in adults, we decided to perform PDCI in children. The first child with PD was implanted at our center in September 2004. To date, there is only one report describing PDCI and EAS in children [32]. The results contained therein demonstrate that some hearing could be preserved in all children with PD, and that furthermore 8 out of 9 children had functional hearing preservation (a rate of 88%). Functional preservation implies that the individuals can be fitted both electrically and acoustically in the same ear, or can use their preserved natural low-frequency hearing to optimize the use of EAS.

Methods

Subjects
Between September 2004 and December 2007, 15 children with PD and 10 platinum HA users were implanted with either a COMBI 40+ or a PULSAR, using the ‘round window’ technique to increase the likelihood of hearing preservation. Results from the first 9 PDCI children have been reported separately [32]. All subjects were implanted in the ear with the worse hearing. The mean age at implantation in the PD group was 9.5 years (ranging from 4.2 to 16.6 years) and in the platinum HA user group the mean age was 9.37 years (ranging from 6.96 to 14.72 years). The reported etiologies were as follows: unknown (n = 13), hypoxia (n = 5) and ototoxicity (n = 7). The PDCI children were implanted using 20-mm partial insertion of a 30-mm-long standard electrode (n = 2) as well as full insertion of a 20-mm M-electrode (n = 13). A limited insertion depth was used in order not to interfere with the region in the cochlea that is associated with good acoustic low-frequency hearing. The platinum HA users were implanted using full insertion of a standard electrode (n = 7) or FLEX electrode (n = 3) because they had less low-frequency hearing. All children had at least 1 year of experience of using the device.

Surgery
The same round window surgical technique [12] was used to ensure hearing preservation in all subjects. This technique has six main steps:

1. mastoidotomy;
2. posterior tympanotomy to allow visualization of the round window niche;
3. puncturing the inferior part of the round window membrane, thus enabling a direct approach to the scala tympani;
4. insertion of the electrode array;
5. fixing the electrode in the round window niche with fibrin glue (the membrane must be left partially uncovered to preserve its mobility), and
6. fixing the device in a well that is made in the temporal bone.

It may be more difficult to insert the electrode in children than in adults because of the short distance between the facial nerve canal and the annulus fibrocartilagineus of the tympanic membrane. For this reason, an anterior tympanotomy is performed more frequently in children than in adults, in order to improve visualization of the round window niche. It is also necessary to close the mastoid with Spongostan, fibrin glue and a piece of bone obtained during the mastoidectomy.

Programming
The speech processor was programmed in such a way that there was a slight overlap with acoustic perception. This means that the low-frequency cutoff point determined by the audiogram lay somewhere between 300 and 1,000 Hz. The low frequencies may then be heard using the subject’s preserved natural low-frequency hearing or using the HA part of the DUET speech processor. The DUET comprises a TEMPO+™ speech processor with precise Hilbert transform envelope detection and a two-channel HA in one unit. Only those electrodes inserted in the cochlea were activated, and electrodes were classified as intra- or extracochlear using impedance telemetry and reports of hearing sensation. The number of active electrodes was usually 8 for the standard and 11 for the medium electrode array in the PDCI group and 11 for the standard and FLEX arrays in the platinum HA user group. The upper frequency end was 8.5 kHz in all cases.

Audiological and Speech Perception Testing
Pure tone testing was performed using a Siemens SD5 audiometer calibrated according to standards established by the American National Standards Institute. Testing was done in an IAC soundproof booth using Sennheiser HDA 200 headphones. A standard clinical procedure was used for determining the thresholds [33].

Subjects were tested using their natural bilateral acoustic hearing and their electrically stimulated hearing
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via the CI in one ear or using a DUET speech processor, if they had been fitted with this. Audiological and speech reception tests under quiet conditions and in speech-shaped noise were performed preoperatively, then at implant fitting, and then at 3, 6, 12, 24, 36 and 48 months after the initial fitting of the device. Speech reception was tested using the Pruszewicz monosyllabic Polish word test (20 words per list, 20 lists) [34], with the lists of words being randomized between test conditions. The Pruszewicz monosyllable test is a consonant-nucleus-consonant test in Polish that is similar to the consonant-nucleus-consonant monosyllabic word test in English. Recorded words were presented in the sound field at 60 dB SPL in quiet and in competition with speech-shaped noise at a speech-to-noise ratio of +10 dB. The results of speech reception tests are the mean values obtained using 3 test lists.

Results

Hearing Preservation
Hearing preservation immediately after the operation was achieved in all 25 children. However, 3 children could be considered as having non-functional partial preservation, because the low-frequency hearing could not be amplified with the HA component of the DUET in the Implanted ear. Overall, hearing loss was not statistically significant for all audiometric frequencies (p > 0.05) either for platinum HA users or for children with PD. The average hearing thresholds, measured before surgery and 1–4 years afterwards, both for the PDCI and for the platinum HA user group, are shown in figure 1. The length of the electrode had no significant effect on the degree of change in the thresholds after surgery.

Speech Perception
Four out of 15 PD children, and 5 out of 10 children from the platinum HA user group could not be assessed using the standard monosyllabic test because it was too difficult for them. For this reason, these 9 subjects were excluded from the speech reception evaluation, leaving 16 subjects with at least 1 year experience of using the device.

The results of monosyllable testing under quiet conditions and under noisy conditions are presented in figure 2. The mean scores and their standard deviations are shown. The postimplant scores after 1 year of CI use exceeded the preimplant scores for all children. Children in both groups performed statistically significantly better with EAS over time under both quiet and

Fig. 1. Preoperative and postoperative audiograms showing the mean and standard deviation for each frequency for two groups of patients. a Children who were platinum HA users preoperatively. b Children with PD.
noisy conditions compared with the preoperative acoustic HA condition. In addition, no significant differences were observed between the two groups under quiet conditions, although under noisy conditions there was a significant difference between the groups at 3, 6, and 12 months after implantation.

**Discussion**

Hearing was preserved and found to be stable over the subsequent 1–4 years in all children implanted using the same round window surgical technique. There was no significant difference in the group comparing preoperative and postoperative thresholds either for children in the platinum HA user group or for children with PD. This was in accordance with the findings of Willingham and Manolidis [28] who used ASSR thresholds to demonstrate that by employing a round window technique in children with residual hearing, there was no statistically significant change in auditory function in the implanted ear after implantation.

In the platinum group of HA users, the rate of functional preservation was 90% (9 out of 10). This result is better than the 71% of children (5 out of 7) with slightly poorer residual hearing previously achieved by the same author using cochleostomy [26].

In the group of 15 children with PD, the rate of functional preservation was 87% (13 out of 15). This is almost the same as the preservation rate of 88% achieved in the subgroup of the first 9 children with PD as previously reported [32]. It is also similar to the preservation rate of 90% achieved in

Fig. 2. Monosyllable scores over time: under quiet conditions in the platinum HA user group (a) and for children with PD (b); under noisy conditions in the platinum HA user group (c) and for children with PD (d). The mean and standard deviation for the electric acoustic conditions are shown.
a group of 10 adult patients with PD [12]. The data support our conclusion that the results from our ‘round window’ hearing preservation technique are repeatable.

There were no significant group differences in the hearing threshold change between children from a platinum HA user group implanted using a full-length 30-mm electrode and children with PD implanted with a shallower 20-mm insertion.

It was decided to use the round window technique instead of cochleostomy because we believed that this would limit the loss of residual hearing. There are known potential problems with cochleostomy, such as (a) perilymph loss and acoustic trauma caused by drilling; (b) formation of new bone within the cochlea, caused by the presence of bone dust [35]; (c) risk of initiating osseous spiral lamina injury, and (d) damage due to infection, which may cause the formation of fibrous tissue [12, 36]. Some authors have used temporal bone studies to address these issues and have demonstrated the supremacy of the ‘round window’ approach over cochleostomy in preventing trauma to cochlear structures [37, 38].

Monosyllabic word recognition increased in the platinum group from 31 to 60% under quiet conditions and from 1 to 19% under noisy conditions over a period of 12 months.

In the PDCI group, the increase under quiet conditions was from 34 to 67% and under noisy conditions from 7 to 47%. These results achieved in the PD group are comparable to the results achieved previously in the subgroup of 9 children (from 30 to 69% under quiet conditions and from 5 to 62% under noisy conditions) [32]. This again confirmed that the results of PDCI are repeatable.

The increase in performance under quiet conditions was comparable in both groups, although the benefit under noisy conditions was significantly greater in the PD group than in the platinum HA user group. This finding reveals that in order to achieve any significant benefit under noisy conditions, good hearing at low frequencies is needed. However, the low number of children tested in the platinum HA user group (n = 5) means that this conclusion should be treated with caution and that further research is needed in this area.

Despite this, the encouraging improvement of speech discrimination under noisy conditions suggests that the benefit from EAS exceeds what usually seen in children who rely on only one CI system [39].

Those subjects who did not demonstrate functional hearing in the implanted ear after surgery were able to obtain a significant advantage by using a CI in one ear and relying on natural low-frequency hearing in the other. This observation is consistent with previous research that suggested that children with asymmetrical hearing loss with open-set sentence scores of above 30%, and up to 87% in the better ear, obtain a significant improvement in speech perception using a combination of ipsilateral electric stimulation via a CI, and contralateral acoustic stimulation, usually using an HA [22].

The significant rapid improvement in auditory capacity, as presented in figures 2, suggests that the gains in performance were due to CI intervention rather than to any progress that would have occurred in the course of rehabilitation with conventional HAs. Further research is needed to assess the role of EAS in the perception of the suprasegmental features of speech and music appreciation in children.

**Conclusion**

The results presented herein indicate that by using the round window approach, it is possible to preserve good low-frequency hearing using a 20-mm insertion depth as well as preserve hearing using a longer 30-mm insertion.

There are two groups of children that may benefit from EAS, namely: (1) children who are platinum HA users preoperatively, who could be
considered as traditional CI candidates, and (2) children with a ski-slope type hearing loss, described herein as PD, whose preoperative hearing thresholds and auditory capacity exceed the normal selection criteria. Children from both groups show rapid improvement in their speech perception abilities after surgery, under quiet and noisy conditions. The parents of these children report a change in both listening behavior and in ease of listening. The same approach was applied in both groups in terms of the type of surgical procedure that was used to try to promote hearing preservation. As a consequence of this, the combination of electric and acoustic stimulation was possible in both groups, and therefore we propose that the term ‘PDCI’ be widened to include children from a platinum HA user group preoperatively, and in broader terms, children with a functional degree of residual hearing. The provision of PDCI opens up the hearing world to these children.

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References


Bilateral Electric Acoustic Stimulation: A Comparison of Partial and Deep Cochlear Electrode Insertion

A Longitudinal Case Study

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Abstract

Background/Aims: A patient with bilateral severe, sloping, high-frequency hearing loss was treated with sequential bilateral electric acoustic stimulation (EAS) using the MED-EL Duet EAS cochlear implant. On one side, a partial 18-mm insertion of the electrode array (M-type) in the cochlea was performed. The contralateral side was implanted 39 months later with a deep 30-mm insertion of the electrode array (FLEXsoft type). The aims were to assess whether low-frequency hearing could be preserved after deep electrode insertion, as well as to assess the benefit of bilateral EAS surgery compared to monaural EAS.

Methods: Hearing thresholds and speech recognition outcomes were measured preoperatively and up to 48 months postoperatively. Outcomes from the partial and deep insertion side are compared. The benefit of EAS in daily life was assessed with the Abbreviated Profile of Hearing Aid Benefit questionnaire. Benefits of bilateral EAS were calculated from speech reception thresholds measured using the LINT speech-in-noise number test. Speech was always presented from the front. Noise was either presented from the front, from the left side, or from the right side. Each condition was measured for unilateral and bilateral EAS use.

Results: Partial as well as deep insertion of the electrode array resulted in hearing preservation and significant speech recognition in this particular case. Both EAS devices provided more than 80% speech recognition in noise at a 10-dB signal-to-noise ratio. Bilateral EAS was beneficial for speech reception in noise compared to monaural EAS. A head shadow effect of 3.4 dB, binaural squelch effect of 1.2 dB and binaural summation effect of 0.5 dB were measured.

Conclusion: Hearing preservation is also possible after cochlear implantation using a FLEXsoft electrode array with a near-full insertion (30 mm) into the cochlea. Bilateral EAS was successfully implemented in this patient providing better speech recognition compared to monaural EAS.

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Electric acoustic stimulation (EAS) combines electric stimulation for the high-frequency range with acoustic amplification for preserved low-frequency hearing. For the purpose of EAS, the electrode array is inserted up to 18–20 mm into the cochlea. Patients using EAS are able to achieve good speech recognition in quiet and in noise [1, 2] despite reports of loss of residual hearing in 17% of patients [3]. A synergistic effect of EAS was first described by von Ilberg et al. in 1999 [4]. The combination of electric and acoustic stimulation of the auditory system provided better speech recognition than
acoustic or electric stimulation alone. This synergistic effect was also found in several other studies [2, 5]. Kiefer et al. [6] reported a synergistic effect in 4 out of 11 patients. For 8 other patients, electric stimulation still provided the largest contribution to speech recognition with EAS. However, unexpected progressive hearing loss may eventually occur after surgery over the years following EAS, and acoustic amplification may not be possible in these patients. The introduction of more advanced hearing preservation techniques for EAS has further increased the chances of preserving residual hearing [7–9]; Gstoettner et al. [3] reported an overall hearing preservation rate of 83.2% and Turner et al. [10] gave evidence for a better frequency resolution of residual hearing, compared to electric stimulation via a cochlear implant (CI). This better frequency resolution could be responsible for better speech recognition observed in EAS users compared to CI users.

Greenwood [11] described the natural acoustic frequency-place coding in the human cochlea in 1961. The natural tonotopy of the cochlea is used in CI technology as well. High-frequency information is conveyed through electric pulses on the electrodes in the base of the cochlea, while more apical electrodes convey low-frequency information. Recently more evidence was provided that the Greenwood function is also applicable for electric stimulation through cochlear implantation [12].

In this paper, we present a case of bilateral EAS with partial insertion on one side and deep insertion on the other side providing preliminary answers to the following questions: Is hearing preservation possible after deep insertion of an electrode when using EAS surgery? Does bilateral EAS provide an additional benefit compared to unilateral EAS combined with contralateral residual acoustic hearing? Does deep insertion of the electrode array improve speech reception using EAS? Is deep insertion of the electrode better than partial 20-mm insertion in EAS?

Research on bilateral CIs shows significant benefits in sound localization [13, 14] and speech perception in noise compared to a monaural CI-fitting [15, 16]. The head shadow effect is responsible for most of the benefit measured in these patients. Schleich et al. [17] found a significant head shadow effect of 6.8 dB, a significant squelch effect of 0.9 dB and a significant summation effect of 2.1 dB in adult bilateral CI users. Bilateral CI users also have better speech recognition in quiet with speech from the front than unilaterally implanted patients [18], which is presumably caused by the effect of binaural summation [19]. To our knowledge, bilateral EAS has not been described in the literature before. Benefits similar to those of bilateral CI use are expected in bilateral EAS users.

**Methods**

**Subject**

A 52-year-old male suffered from bilateral, mid- and high-frequency steeply sloping hearing loss as a result of ototoxic medication for more than 16 years. He was implanted in 2004 on the right side with a MED-EL COMBI 40+ and a medium electrode array inserted up to 20 mm. Cochlear implantation in his left ear was performed 39 months later using a PULSAR<sup>TM</sup> implant with a FLEXsoft electrode inserted up to 30 mm. Postoperatively low-frequency hearing was preserved in both ears in a way that electric stimulation could be combined with acoustic amplification using the MED-EL DUET EAS system.

**Surgical Procedure**

The subject received a MED-EL COMBI 40+ CI with a M-electrode in his right ear using the specific EAS hearing preservation surgical technique [6]. The M-electrode is 20.9 mm long and has 12 stimulation channels, each with double electrode contacts. The contact spacing between electrodes is 1.9 mm.

The highlights of the surgical procedure are described in brief. Prior to the skin incision, intravenous antibiotics and intramuscular 80 mg methylprednisolone were given. After posterior tympanotomy, cochleostomy was performed antero-inferior to the round window using an inferior to superior approach with a slow-drilling 0.9-mm diamond drill until 1.0 mm of the endosteum of the scala tympani was exposed. The cochleostomy was done with the utmost care not to break the spiral lamina or to aspirate perilymph. Triamcinolone 40 mg/kg solution was applied on the endosteum and the round
window membrane for 20 min, during which time the implant bed was drilled and the implant fixed in place. The middle ear was cleaned and irrigated with a ciprofloxacin solution. The endosteum of the scala tympani was sharply opened at the inferior border of the cochleostomy and triamcinolone and hyaluronic acid were reapplied. The M-electrode was very slowly introduced in the scala tympani in an inferior-anterior and medial direction, taking care not to introduce bone dust or blood with the electrode into the scala. The M-electrode was advanced for 20 mm, leaving the 11th electrode pair outside the scala. A piece of fascia sealed off the cochleostomy and was kept in place with fibrin glue (Tissucol™). Methylprednisolone was continued for 14 days in a daily decreasing dosage.

Thirty-nine months after the first implant, the patient received a PULSARCI100 implant with a FLEXsoft electrode on the left side. This electrode has a full length of 31 mm but is extremely flexible, with 5 single electrode contacts distally, and a diameter of 0.3 mm at the tip. This electrode design reduces the insertion force, decreases the intracochlear fluid insertion pressure and reduces the intracochlear and cochleostomy trauma. The same surgical procedure was used as on the right side, except for the depth of insertion. The electrode was inserted up to the first point of resistance which was at 30 mm.

**Results**

**Hearing Preservation**

In figure 1, preoperative and postoperative acoustic hearing thresholds are shown for the patient’s right ear at each test interval up to 48 months of EAS use and for his left ear up to 12 months of EAS use. There seems to be a slight progressive hearing loss in the right ear. One year postoperatively, the maximum difference in hearing thresholds in the right ear was 15 dB at 250 Hz, 4 years postoperatively the maximum threshold shift was 30 dB at 250 Hz. Functional hearing preservation was achieved after deep insertion on the left side. The maximum hearing threshold shift in this ear was 15 dB at 250 Hz and 1,000 Hz 18 months postoperatively. The average hearing loss in the right ear 48 months after EAS use for the frequencies 125, 250 and 500 Hz was 22 dB; the average hearing loss in the left ear was 10 dB at these frequencies 18 months after surgery. Preservation of both low-frequency hearing and residual high-frequency hearing was achieved.

**Speech Recognition**

Speech recognition of monosyllables using EAS in the right ear improved from 25% preoperatively to 66% after 12 months of EAS use. Testing each year thereafter revealed a further improvement up
to 75% after 48 months of EAS use. For sentences in quiet, speech recognition improved from 46% preoperatively to 98% after 12 months of right EAS use. Sentences in noise scores improved from 2% preoperatively to 89% after 12 months of right EAS use and remained stable at 90% for the next 3 years. Overall results of speech recognition after 18 months of left EAS use were 50% for monosyllables and 88% and 81% for sentences in quiet and in noise, respectively.

The results for speech recognition in noise and in quiet are given in figure 2, showing scores for EAS as well as HA, CI fitted for the full frequency range and CI fitted for the EAS range. The speech recognition scores were higher in the right EAS condition than in the CI- or HA-only conditions. Left EAS in quiet also provided better speech recognition than the CI- or HA-only conditions during the first 3 months of EAS use. After 6 months, the CI in the full frequency fitting range provided 18% more speech recognition in quiet than the EAS system. An additive or synergistic effect could not be revealed, meaning the speech recognition scores using EAS were not higher than that of CI-only and HA-only added up.

Bilateral Electric Acoustic Stimulation
This patient received bilateral EAS of the cochlea. The added value of bilateral fitting of EAS compared to monaural EAS was investigated. Bilateral EAS yielded lower SRT’s in noise than using either of the EAS devices separately. SRT’s up to −9 dB SNR were measured. Head shadow effect, binaural squelch and summation effect are shown in figure 3 together with the speech reception results. An average head shadow effect of 3.4 dB was measured. Binaural summation was 0.5 dB, and a squelch effect of 1.2 dB was found for this patient.

Self-Assessment of Hearing Difficulties
The subjective benefit of EAS compared to the preoperative HA condition was measured using the APHAB questionnaire. Figure 4 shows the total score and subscores of the APHAB questionnaire for each test interval. The patient’s perception of his disability led to a reduction with EAS use, which continued even up to 48 months after the first implantation. The addition of the contralateral implant caused a further increased benefit, reflected in the assessment after 48 months of EAS use. A negative effect of the second EAS implant
was measured for the subscore for aversiveness – loud sounds are more uncomfortable when using bilateral EAS. The patient also reported an increased sense of security, knowing that in case of a further deterioration of low-frequency acoustic hearing, the left CI could be refitted to electrically stimulate the complete cochlea.

**Discussion**

Attempts to preserve residual acoustic hearing using a standard or medium length electrode that is partially inserted into the cochlea, combined with hearing preservation techniques are described by several research groups. In 2004, Gstoettner et al. [5] were able to preserve residual hearing in 18 of
21 patients. Kiefer et al. [6] reported an average hearing loss of 15 dB at lower frequencies in 11 out of 13 patients; however, in 2 patients residual hearing was lost. In a study by James et al. [25], insertion depth varied between 17 and 19 mm. They reported an average loss of 25 dB in the lower frequencies for 12 patients, including 2 patients with a complete loss of residual hearing.

For the patient described in this article, hearing preservation was achieved after bilateral cochlear implantation using hearing preservation surgery. After partial insertion of a MED-EL M-electrode in the right cochlea, residual hearing remained relatively stable up to 48 months after implantation. Hearing preservation was also achieved in the left ear after a deep insertion of a standard length FLEXsoft electrode. These results show that hearing preservation is possible after careful cochlear implantation using deep insertion of a flexible and thin electrode array, following strict hearing preservation procedures.

Deep insertion might be an alternative for patients with residual hearing that can be used for acoustic amplification when progressive hearing loss cannot be ruled out. If residual hearing is lost after CI surgery, the CI can be fitted for the full frequency range, electrically stimulating the complete cochlea. However, with deep insertion the risk of damaging the cochlea and losing residual hearing is presumed to be higher, with limited hearing preservation success being reported in the literature [5].

A synergistic effect of combining electric and acoustic stimulation could not be revealed in our patient. The absence of a synergistic effect could be explained by the high speech recognition scores achieved with CI-only (up to 87% in noise). Speech recognition in quiet and in noise using the right EAS device was higher than in CI- or HA-only conditions. However, there was little difference between EAS and CI-only fitted for the EAS range. For the left ear there was not much difference between EAS and CI-only conditions either. The CI contributed towards a large part of the speech recognition scores, regardless of the fitting range or combination with acoustic stimulation.

Although preoperative hearing threshold levels are higher in the left ear, the left CI seems to
provide more speech recognition on its own than the right CI alone. A possible explanation for this might be that with deep insertion of the electrode array the place of electric stimulation corresponds better with the natural acoustic frequency-place coding of the auditory system first described by Greenwood [11]. Another factor that might contribute to a better speech recognition is the difference in contact spacing between electrode pairs. In the M-electrode array, the spacing between electrode pairs is 1.9 mm compared to a wider contact spacing of 2.4 mm between electrodes in the FLEXsoft electrode array. Wider spacing between electrodes is supposed to reduce the amount of channel interaction in the cochlea and can improve speech reception [26].

Bilateral EAS seems to be especially beneficial in noisy listening situations with improved SRT’s due to head shadow, squelch and summation effects. Head shadow, squelch and summation effects could be measured in this patient, but these effects are smaller than in normal-hearing listeners.

Subjective hearing benefit in daily life measured with the APHAB questionnaire improved after first and second EAS implantation. Even over longer time periods, this improvement continued. Additional EAS in the left ear also resulted in an improved hearing benefit in daily life. The worsening of the aversiveness score, with the sound becoming too loud in the bilateral condition, may reflect some form of loudness summation and needs to be considered in the fitting. In CI users substantial amounts of loudness summation have been reported [27]. With bilateral EAS, fitting procedures should be similar to a standard EAS fitting procedure taking into consideration that with the additional EAS, some sounds could sound too loud.

**Conclusion**

Hearing preservation was achieved after both CI surgeries using specific techniques designed to be atraumatic for the cochlea. Even with full insertion of a FLEXsoft electrode into the cochlea, with an insertion depth of 30 mm, residual acoustic hearing was preserved in this patient by taking into account special measures during and after surgery to avoid the loss of residual hearing. EAS can provide good speech recognition in quiet and
in noise for patients with sloping high-frequency hearing loss. Bilateral EAS is especially beneficial in noisy environments with improved speech reception due to head shadow, squelch and summation effects. Also, the perceived hearing disability in daily life decreased after first and after contralateral implantation, showing a benefit of EAS compared to preoperative hearing, and of bilateral EAS compared to unilateral EAS. The success rate of hearing preservation with a deep insertion of an electrode and the benefits of bilateral EAS still need to be further investigated for possible use in the future.

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