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Clinical Trial on the Capacitive Component of Electrical Impedance in the Cochlea and the Effect of Topical Dexamethasone in Cochlear Implant Surgery

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A R G E N T I N A

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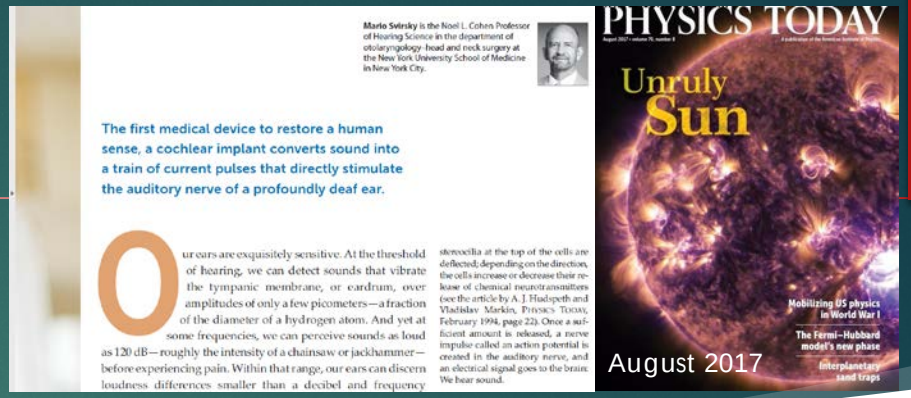
Disclosure

- F. Di Lella is a Latin-American Medical Consultant for:
  - Cochlear Ltd.
  - Advanced Bionics

Introduction



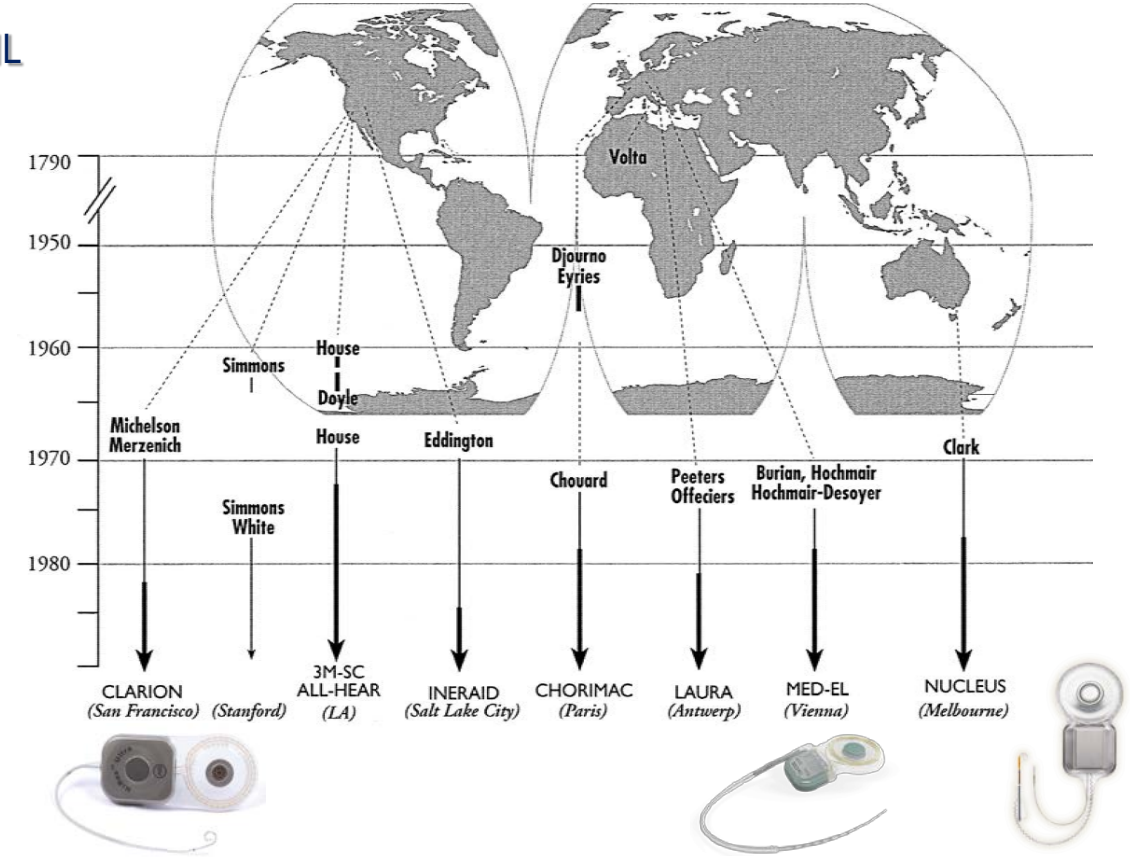
Cochlear implants The first medical device to restore a human sense

- Feasible and secure treatment for severe to profound SNHL
- **Speech perception outcomes may vary due to:**

Biographical factors
- Age
- Genetics
- Immunological response
- Cochlear anatomy

Audiological factors
- Onset of Hearing impairment
- Etiology of HL
- Residual hearing

Surgical factors
- Cochlear approach (RW, eRW, Co)
- Insertion trajectory
- Insertion speed
- Electrode (flexibility, dimensions)
- Depth of insertion
- Blood / Bone dust



Potential Damages inside the Cochlea with a CI

Surgical Approach

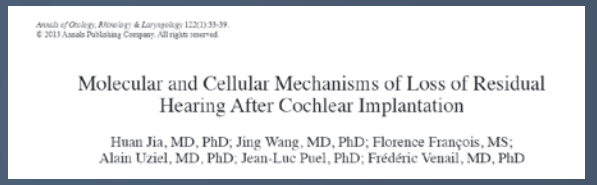
- Opening of the cochlea: endosteal lesions, bleeding, bone dust, perilymph suction (ACTIVATE THE COCHLEAR INFLAMMATORY CASCADE)
- Insertion of the electrode array: damage to the lateral wall, modiolar damage, damage to the basilar membrane, scala dislocation (INTRACOCHLEAR STRUCTURAL DAMAGE)

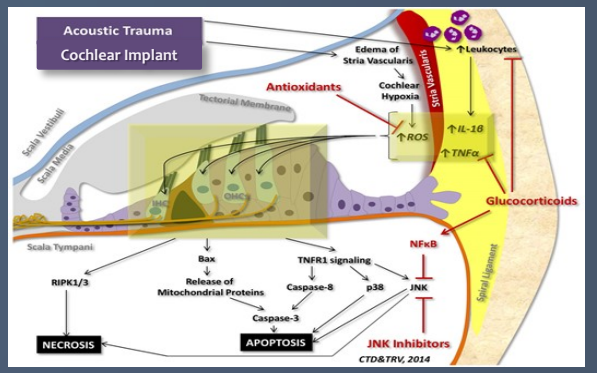
Acute inflammatory reaction

- Cytokines and free radicals
- Hair cells and neuronal damage: apoptosis - necrosis

Chronic inflammatory reaction

- Labyrinthitis, progressive intracochlear fibrosis, ossification





There are evidences that cochlear damage is not good...

M. L. CARLSON ET AL.

A. DALBERT ET AL.

Otology & Neurotology
32:962–968 © 2011, Otology & Neurotology, Inc.

2011 - USA

Implications of Minimizing Trauma During Conventional Cochlear Implantation

Matthew L. Carlson, Colin L. W. Driscoll, René H. Gifford, Geoffrey J. Service, Nicole M. Tombers, Becky J. Hughes-Borst, Brian A. Neff, and Charles W. Beatty

Department of Otolaryngology Head and Neck Surgery, Mayo Clinic School of Medicine, Rochester, Minnesota, U.S.A.

ily focused on the incidence and sustainability of postoperative preserved hearing and the benefit of EAS. However, in the present study, we test the hypothesis that patients sustaining less intracochlear trauma during implantation with a conventional length electrode will demonstrate improved speech understanding in the electric-only condition. If substantiated, the results of this study would support the argu-

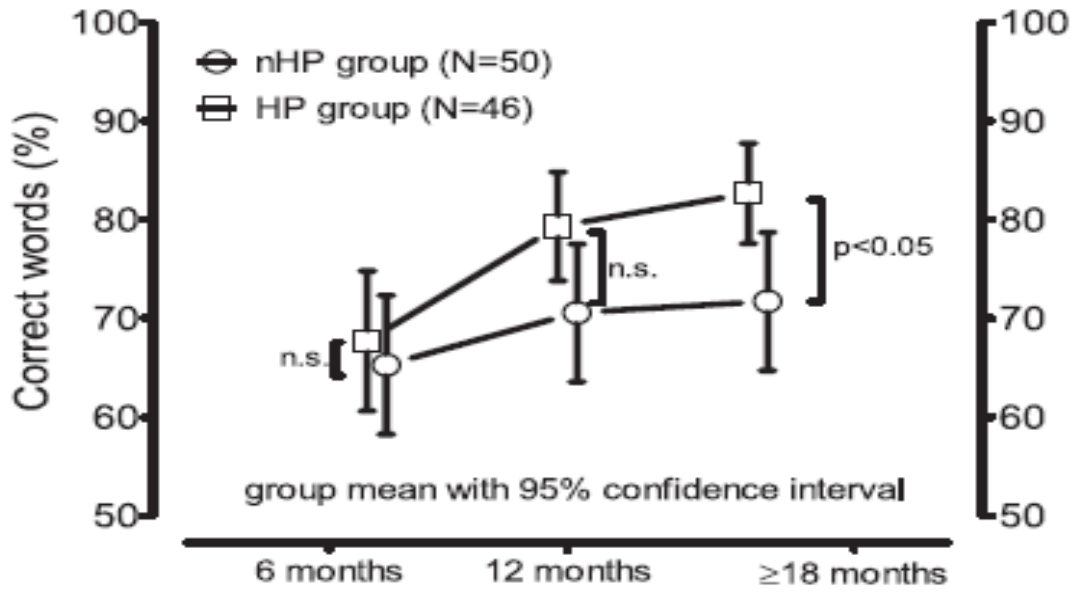
Otology & Neurotology
37:1314–1319 © 2016, Otology & Neurotology, In

2016 - Switzerland

Hearing Preservation After Cochlear Implantation May Improve Long-term Word Perception in the Electric-only Condition

*†Adrian Dalbert, *†Alexander Huber, *†Naemi Baumann, *†Dorothe Veraguth, *†Christof Roosli, and *†Flurin Pfiffner

**University of Zurich; and †Department of Otorhinolaryngology—Head and Neck Surgery, University Hospital Zurich, Zurich, Switzerland*



Impact of Perioperative Oral Steroid Use on Low-frequency Hearing Preservation After Cochlear Implantation

Alex D. Sweeney, Matthew L. Carlson, M. Geraldine Zuniga, Marc L. Bennett, George B. Wanna, David S. Haynes, and Alejandro Rivas

The Otology Group of Vanderbilt University, Department of Otolaryngology–Head and Neck Surgery, Vanderbilt University Medical Center, Nashville, Tennessee, U.S.A.

COCHLEAR IMPLANTS INTERNATIONAL, Vol. 11 Supplement 1, June, 2010, 42–55

Conservation of Hearing and Protection of Auditory Hair Cells against Trauma-Induced Losses by Local Dexamethasone Therapy: Molecular and Genetic Mechanisms

THOMAS R VAN DE WATER, RALPH N ABI HACHEM, CHRISTINE T DINH, ESPERANZA BAS, SCOTT M HAAKE, GIA HOOSIEN, RICHARD VIVERO, SHERRY CHAN, JAO HE, ADRIEN A ESHRAGHI, SIMON I ANGELI, FRED F TELISCHI, and THOMAS J BALKANY

Cochlear Implant Research Program, University of Miami Ear Institute, Department of Otolaryngology, University of Miami Miller School of Medicine, Miami, FL 33136-1015, USA

Research paper

The role of extended preoperative steroids in hearing preservation cochlear implantation

Jafri Kuthubutheen [a, b, *], Harvey Coates [b], Corwyn Rowsell [c], Julian N
Joseph M. Chen [a], Vincent Lin [a]

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Hearing preservation using topical dexamethasone alone and associated with hyaluronic acid in cochlear implantation

BERNARDO FARIA RAMOS, ROBINSON KOJI TSUJI, RICARDO FERREIRA BENTO, MARIA VALERIA SCHMIDT GOFFI-GOMEZ, HENRIQUE FARIA RAMOS, PAOLA ANGELICA SAMUEL & RUBENS BRITO

Department of Otolaryngology, University of São Paulo School of Medicine, São Paulo, Brazil

Effect of Embedded Dexamethasone in Cochlear Implant Array on Insertion Forces in an Artificial Model of Scala Tympani

*†‡Yann Nguyen, *†‡Daniele Bernardeschi, *Guillaume Kazmitcheff, *Mathieu Miroir, *Thomas Vauchel, *†‡Evelyne Ferrary, and *†‡Olivier Sterkers

The Laryngoscope

The Role of Preoperative, Intratympanic Glucocorticoids for Hearing Preservation in Cochlear Implantation: A Prospective Clinical Study

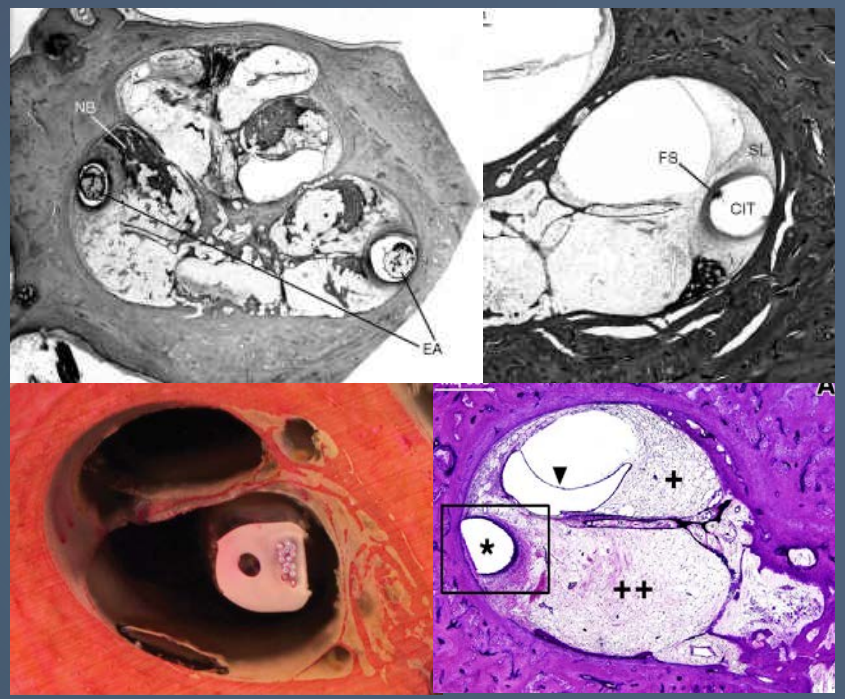
Gunesh P. Rajan, MD, DM, FSCS, FRACS; Jafri Kuthubutheen, MBBS, FRACS; Naveen Hedne, MBBS; Jay Krishnaswamy, M.Sc.Aud

Introduction

The electrode array in the cochlea:

A BENEFIT for the patient & a PROBLEM for the cochlea

How the cochlea reacts to the implant
inflammatory response → fibrosis → ossification



Distance to the modiolus

- The Electro-Neural Interface:
  - The electrode surface
  - The stimulus parameters
  - **The nature of the medium**

Impedances

- Assess electrode functioning
- Calculate power consumption
- Kinking of flexible electrodes
- Mapping

May vary over time (protein adsorption, cellular inflammatory reaction, fibrosis, ossification)

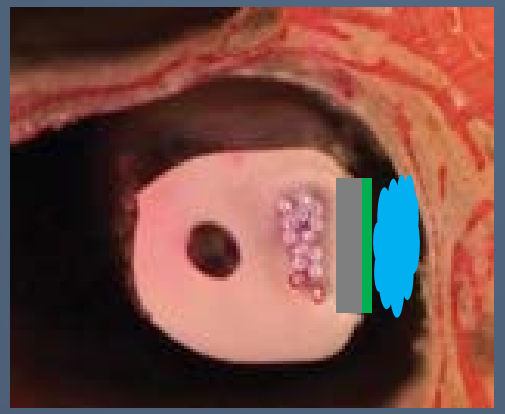
Newbold, C. *et al.* Changes in biphasic electrode impedance with protein adsorption and cell growth. J. Neural Eng. 7, 056011 (2010).

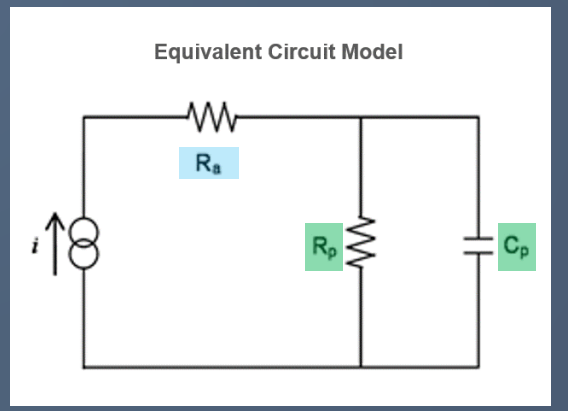
Introduction

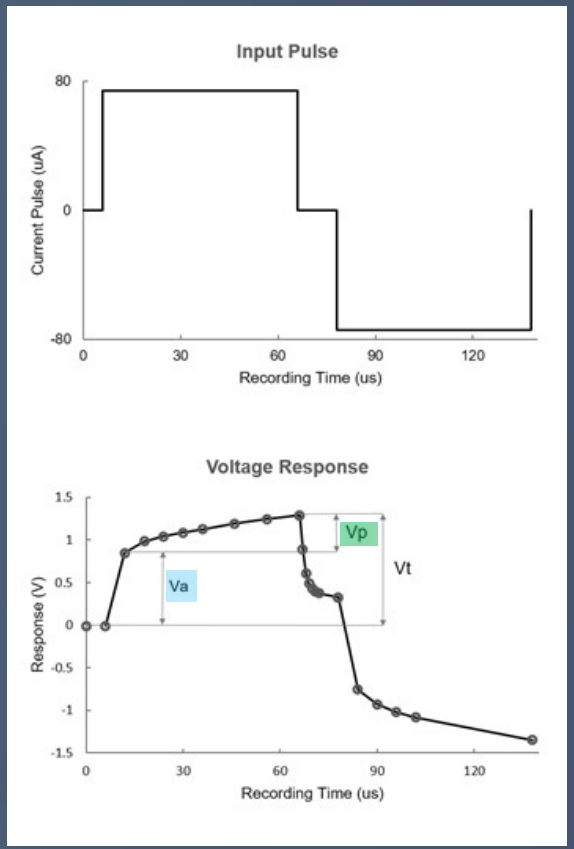
- Cochlear implants are unable to directly assess impedance.
- Impedances can be obtained by measuring voltage, as provided by Ohm's law. (Z = V / i)
- The current clinical method of monitoring electrode impedance in patients can only determine the overall electrode impedance (Zt)

$$Zt = Za + Zp$$

$$Zt = \frac{Va}{i} + \frac{Rp\left[1 - e^{\left(\frac{-t}{Rp*Cp}\right)}\right]}{i}$$







Tykocinski, M., Cohen, L. T. & Cowan, R. S. Measurement and analysis of access resistance and polarization impedance in cochlear implant recipients. Otol. Neurotol. 26, 948–956 (2005).

Objective

- Evaluate the effect of the use of a ***single dose topical dexamethasone*** during CI surgery with ***a novel daily in-vivo real-time remote method to measure and calculate overall electrode impedance and its subcomponents in cochlear implant recipients***.

Material & Methods

Clinical Trial
Randomized, double-blind, placebo-control study

Control Group
n = 10
Saline Solution

20 patients
Profound SNHL
CI candidates

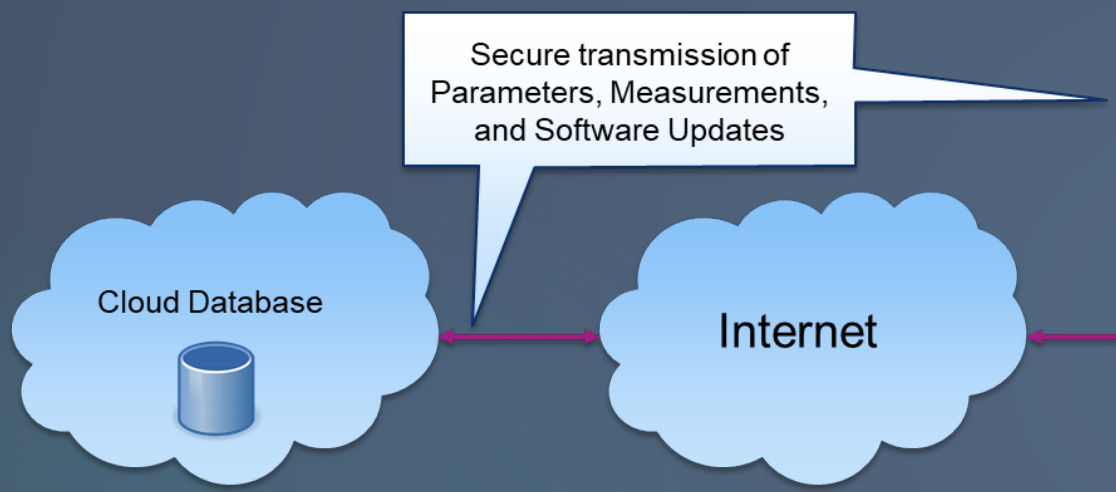
Intervention Group
n =10
Dexamethasone 20 mg/ml

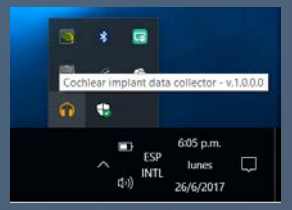
Cochlear Nucleus CI24RE CA / CI512
Contour Advance electrode array

This study was approved by the Human Research and Ethics Committee at the Hospital Italiano de Buenos Aires, IRB00010193

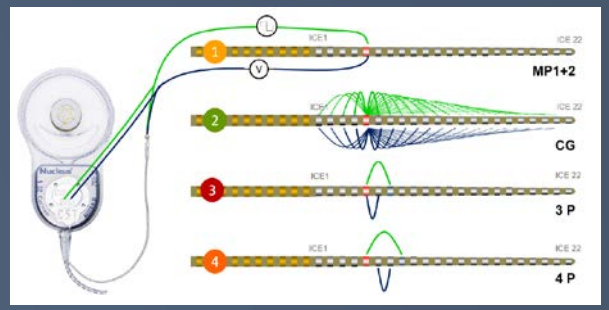
Cochlear Implant Data Collector Software (CIDC)

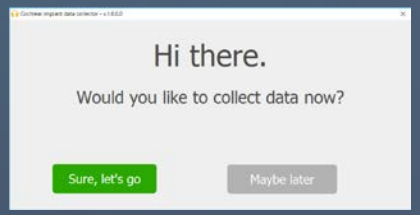
Patients are instructed to measure themselves 2 times per day from the day of surgery to the day of activation

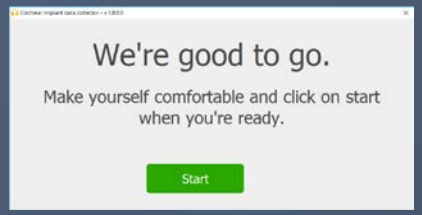


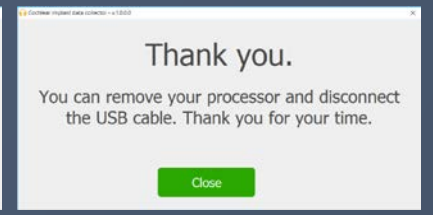


Patient 1

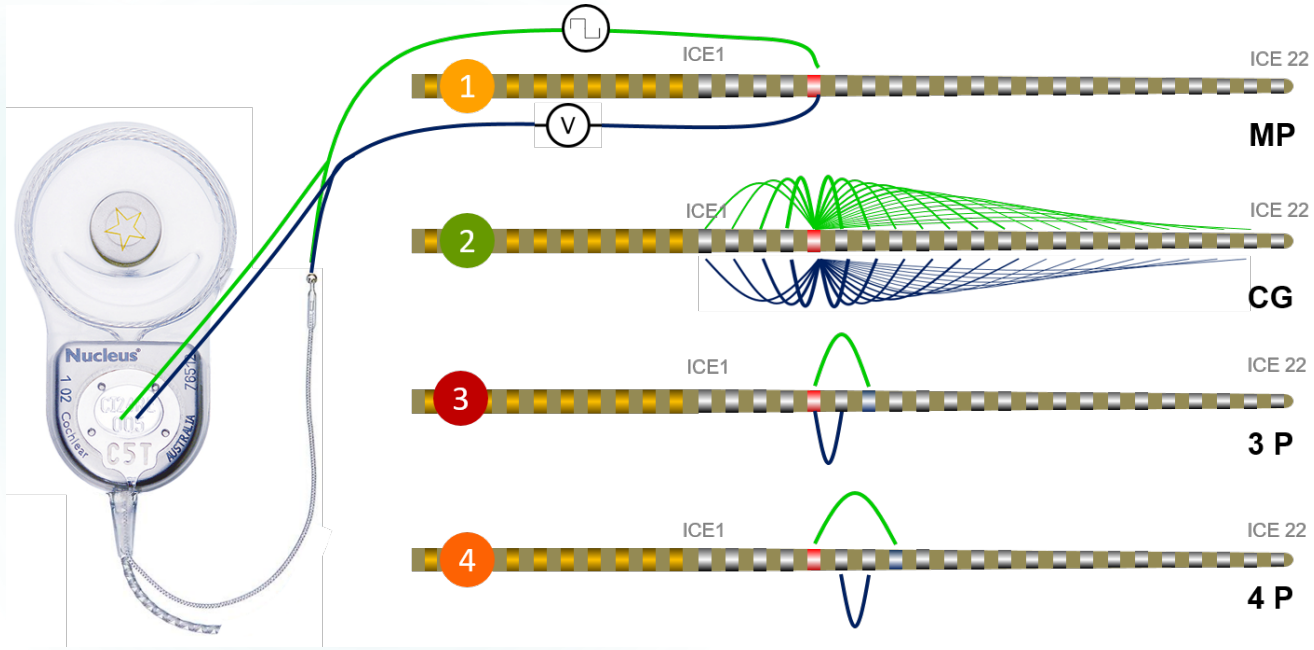




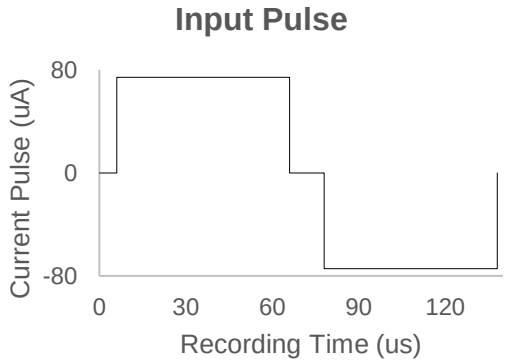




Stimulation Modes & Measurement Sequences



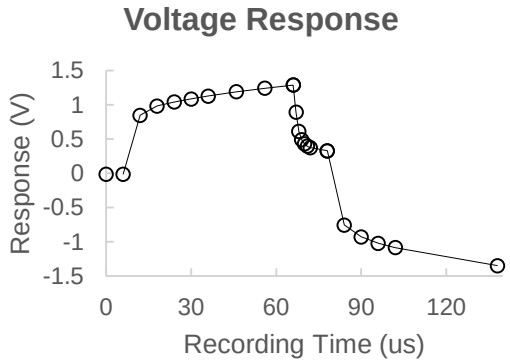
Stimulus parameters:
- ❑ Current level: 80 (74.21 uA)
- ❑ Pulse width: 60 uS
- ❑ Inter-phase gap: 12 uS
- ❑ Period: 333.4 uS (freq. 3 KHz)



Voltage measurements:
- ❑ 22 measurements / input pulse
- ❑ 4 modes
- ❑ 22 electrodes

1936 values

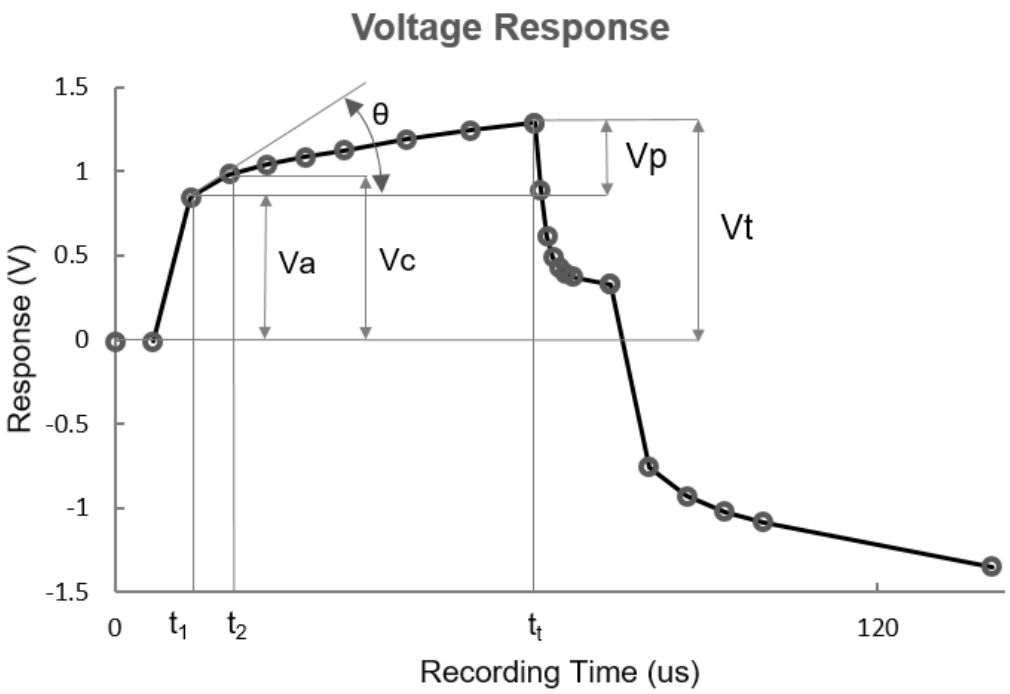
~ 5 minutes



Cochlear Implant Data Analyzer Software (CIDA)

Automatic calculation of Access Resistance and Polarization Impedance

Di Lella et al. Otology & Neurotology: June 2019 - Volume 40 - Issue 5S - p S18–S22



$$Va = i * Ra \rightarrow \boxed{Ra = \frac{Va}{i}} \quad (1)$$

$$\tan\theta = \frac{Vc - Va}{t_2 \_ t_1}$$

$$Cp = \frac{i}{\tan\theta}$$

$$\boxed{Cp = i * \frac{(t_2 - t_1)}{Vc - Va}} \quad (2)$$

$$\boxed{Vt = i * Ra + i * Rp \left[1 - e^{\left(\frac{-t_t}{Rp * Cp}\right)}\right]} \quad (3)$$

Ra, Cp, Rp

Original Study

In Vivo Real-time Remote Cochlear Implant Capacitive Impedance Measurements: A Glimpse Into the Implanted Inner Ear

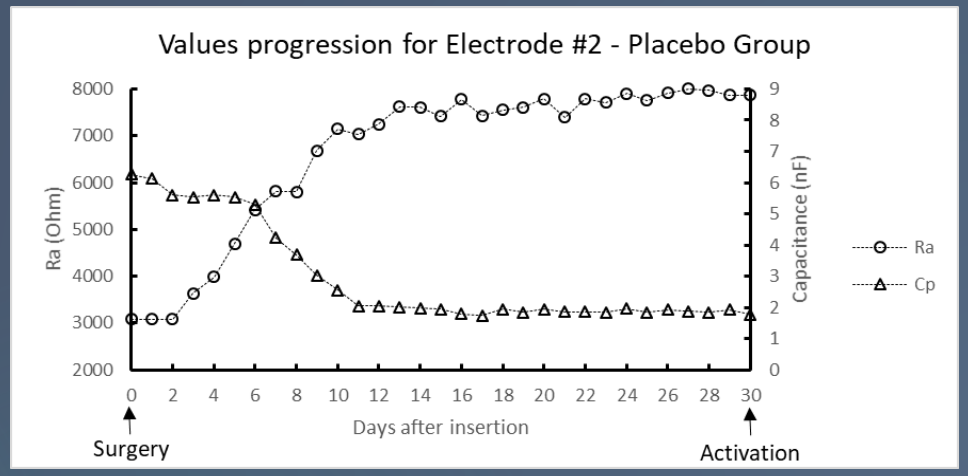
Federico Alberto Di Lella, Diego De Marco, Florencia Fernández, Matías Parreño, and Carlos Mario Boccio

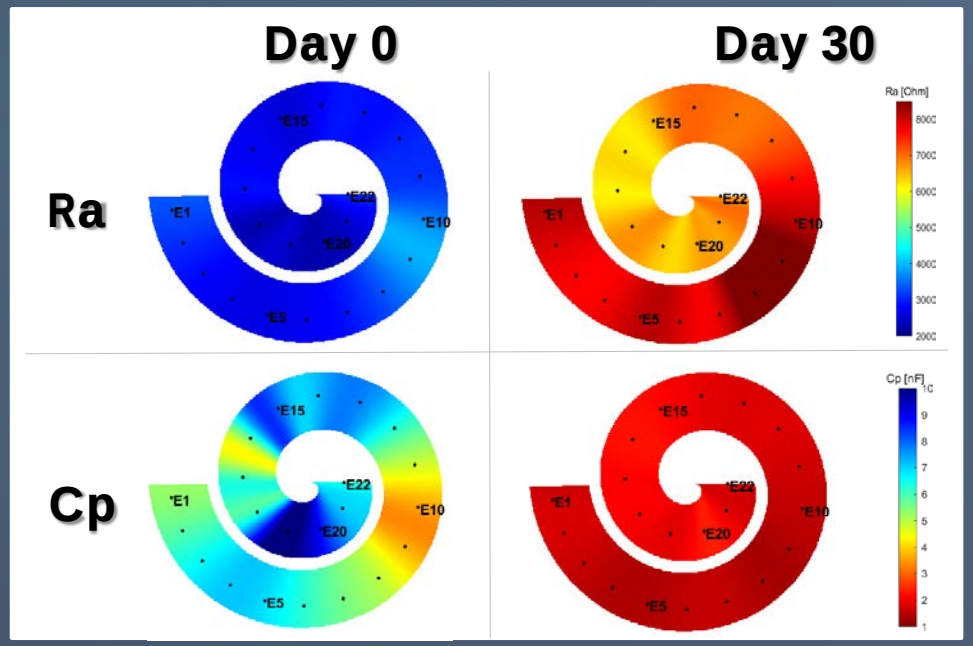
Otorhinolaryngology Department, Hospital Italiano, Buenos Aires, Argentina

Otol Neurotol 40:S18–S22, 2019

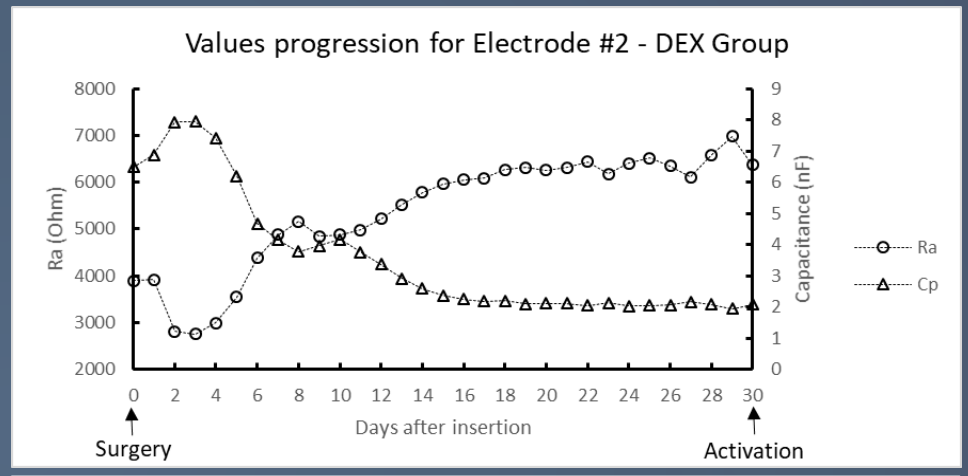
Results: Definite pattern progression

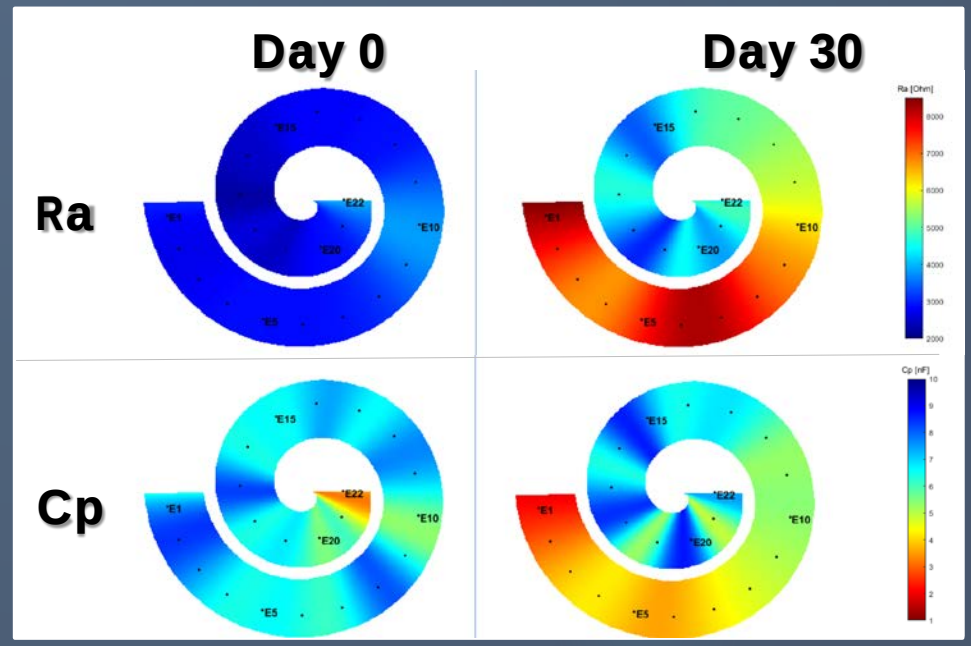
PLACEBO





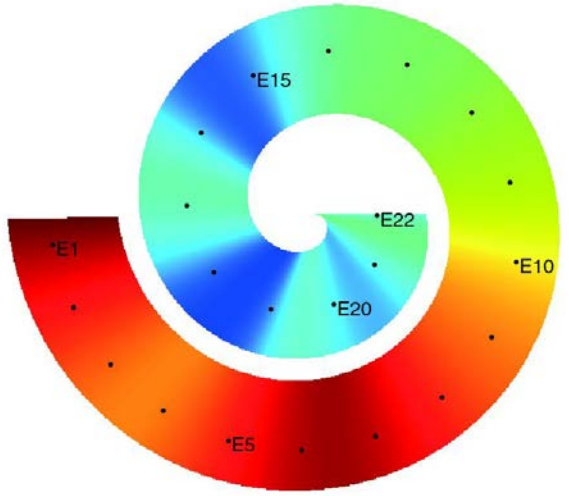
DEXAMETHASONE





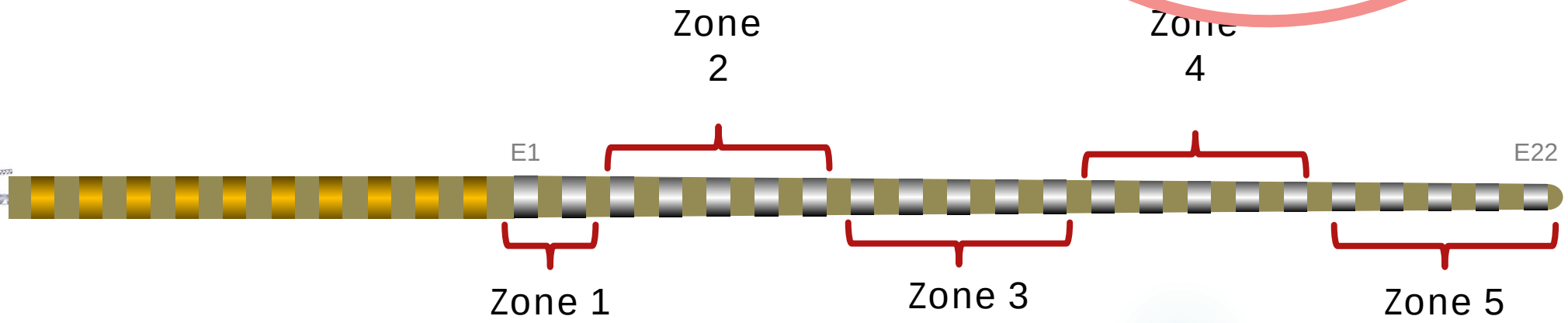
Results

Zone 1: electrodes 1 & 2
Zone 2: electrodes 3 to 7
Zone 3: electrodes 8 to 12
Zone 4: electrodes 13 to 17
Zone 5: electrodes 18 to 22



Basal

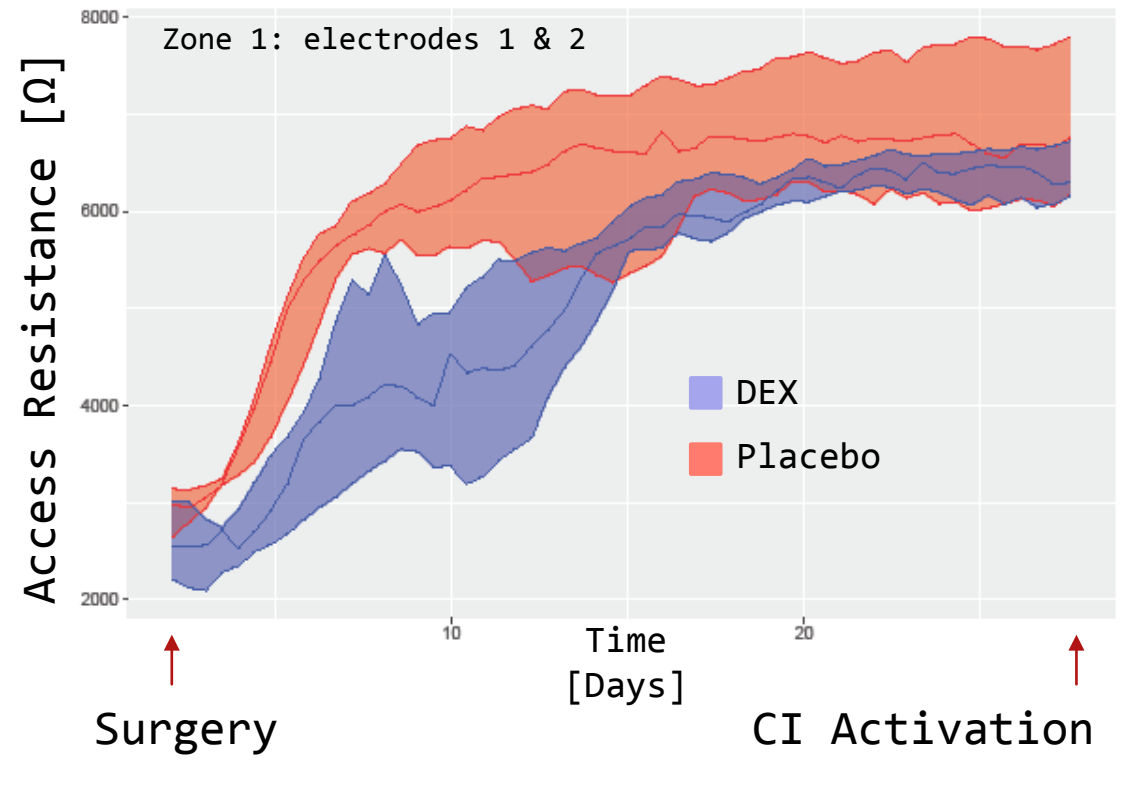
Apical

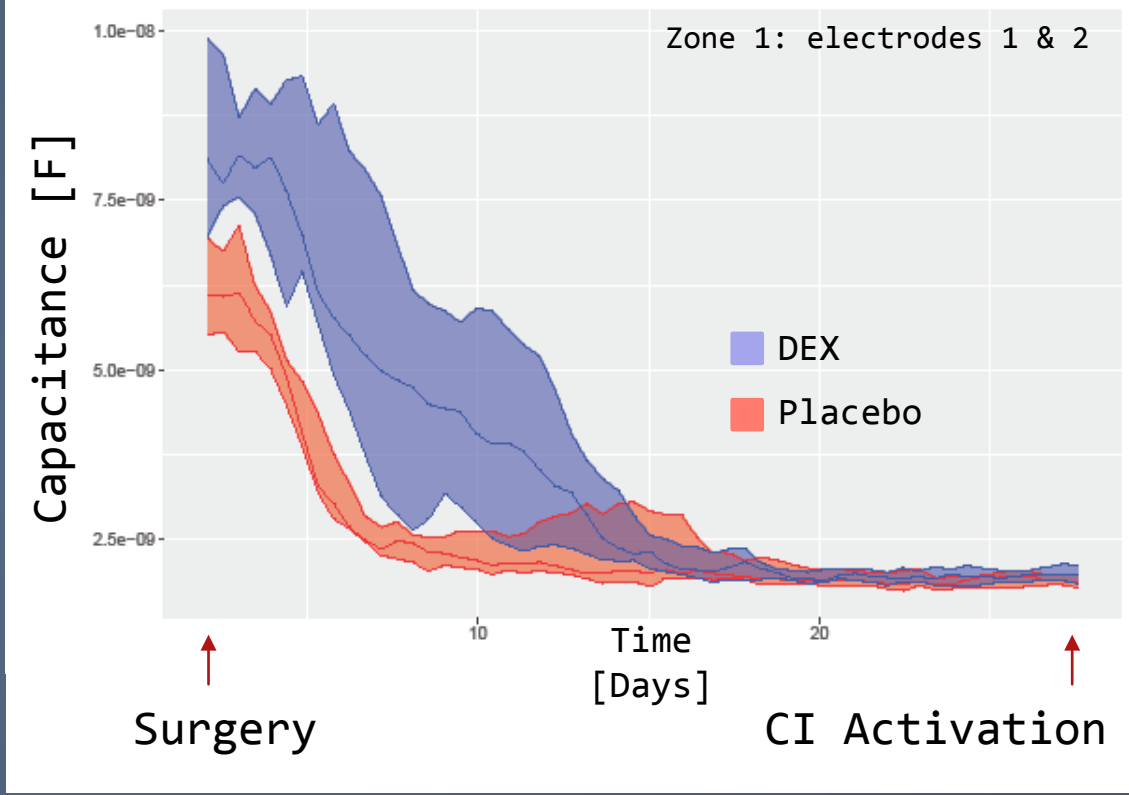


Changes are more important at the level of the basal turn of the cochlea (electrodes 1 & 2), which resulted in dividing the cochlea into 5 zones for the study

Zone 1: electrodes 1 & 2.
Zone 2: electrodes 3 to 7.
Zone 3: electrodes 8 to 12.
Zone 4: electrodes 13 to 17.
Zone 5: electrodes 18 to 22.

Results





- Groups comparison using Shen & Faraway test.
- There seems to be significant differences in basal electrodes (1 & 2) between both groups for both Ra and for Cp ($p < 0.05$)
- This difference seems to be only observable during the first 10 days postimplantation, to later reach similar values in both group.

Zona 1	Zona 2	Zona 3	Zona 4	Zona 5
0.0381	0.5595	0.9536	0.1957	0.1008

$p-$valores del Test de Shen-Faraway para la variable **ra**

Zona 1	Zona 2	Zona 3	Zona 4	Zona 5
0.0136	0.0821	0.2126	0.0815	0.1527

$p-$valores del Test de Shen-Faraway para la variable **cp**

Discusion

- The **inflammatory response** produced after cochlear implantation promotes **fibrotic tissue** deposition around the electrode array which can also **impair electrode impedance and post implantation hearing outcomes**.
- **Protein adsorption** onto the material surface is the first reaction that occurs to medical devices implanted in the body (Tang and Eaton 1999, Shen and Horbett 2001), and same reaction is observed for electrodes implanted into the fluid-filled scala tympani of the cochlea. Such adsorption of protein is also likely to **increase electrode impedance**. Newbold et al (2010) demonstrated that protein adsorption **increased the polarization component** of electrode impedance when measured with biphasic current pulse. Franks et al (2005) showed that coatings of laminin and poly-l-lysine on platinum electrodes resulted in a **reduction of the capacitance measure**, thereby increasing the overall electrode impedance.
- Choi *et al.* (2017) reported that a rise of electrode impedance would likely start in the basal turn of the cochlea.

Discusion

Good correlation between impedances and intracochlear fibrosis

RESEARCH ARTICLE

Impedance Changes and Fibrous Tissue Growth after Cochlear Implantation Are Correlated and Can Be Reduced Using a Dexamethasone Eluting Electrode

Maciej Wilk[1,2☯], Roland Hessler[3☯], Kenneth Mugridge[3], Claude Jolly[3], Michael Fehr[2], Thomas Lenarz[1,4], Verena Scheper[1,4]*

1 Department of Otolaryngology, Hannover Medical School, Hannover, Germany, **2** Clinic for Exotic Pets, Reptiles, Pet and Feral Birds, University of Veterinary Medicine, Foundation, Hannover, Germany, **3** MED-EL GmbH, Innsbruck, Austria, **4** Cluster of Excellence "Hearing4all", Hannover Medical School, Hannover, Germany

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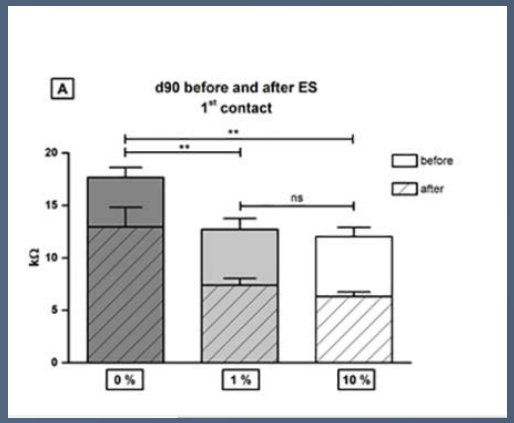

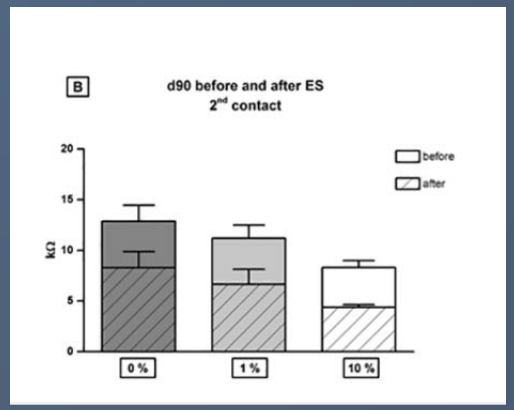

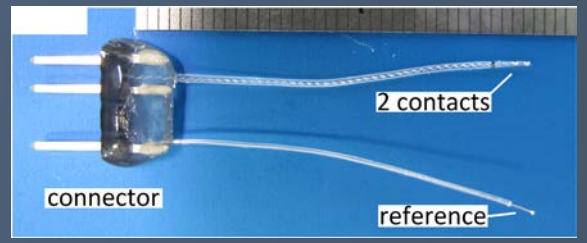

The highest levels of fibrous tissue growth were detected in the basal region of the cochlea, in the vicinity of the round window niche

Conclusions

- This **method** has proven to be **useful** for the safe and **remote assessment of the electrical impedance components in cochlear implant recipients.**
- **Single dose of topical dexamethasone during CI surgery seems to be useful to modulate the inflammatory reaction only in the basal turn of the cochlea and only for the first postoperative week.**
- **Ra** values could help to better understand the **fibrosis reaction inside** the cochlea. We confirm a significant increase in Ra from the surgery to the CI activation, specially on the basal turn of the implanted cochlea.
- **Polarization impedance**, specially measured by **Cp**, may provide important information about the **initiation** of the complex inflammatory response that occurs inside the implanted cochlea.

Further developments

- Use of patient-administered impedance tests for long term cochlear health assessment after cochlear implants is a promising field to improve outcomes and also for drug effect monitoring.

- A multi-center clinical trial to evaluate daily impedance changes with the use of systemic steroids and also the correlatation with hearing preservation is currently on development at our center. Results will be available shortly.

Thank you for your attention

Di Lella, Federico A; Fernandez, Florencia; Parreño, Matias & Boccio, Carlos M

HOSPITAL ITALIANO de Buenos Aires
150 años de vida

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