



# Sensorion KOL Webinar SENS-401 to Prevent Residual Hearing Loss after Cochlear Implantation

July 5, 2023

# DISCLAIMER

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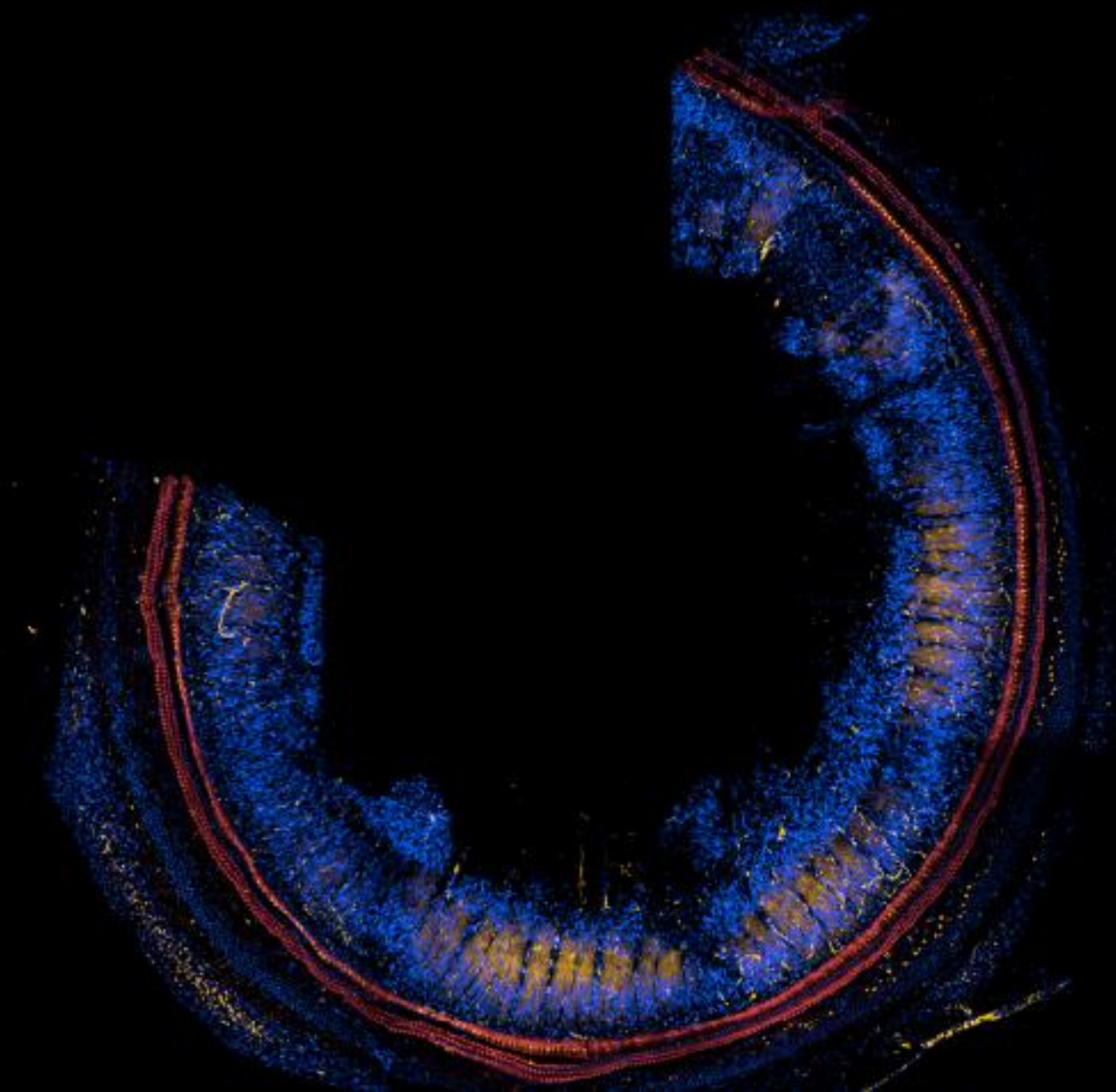
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## WELCOME AND INTRODUCTION

| Nawal Ouzren  
CEO, Sensorion

July 5, 2023



# Agenda

**Nawal Ouzren** – Sensorion

**Yann Nguyen** – Pitié Salpêtrière Hospital

**Géraldine Honnet** – Sensorion

- **Welcome and Introduction**
- **Why Hearing Preservation is Important for Cochlear Implantation**
- **Sensorion's Phase 2a Study Preliminary Results Overview**

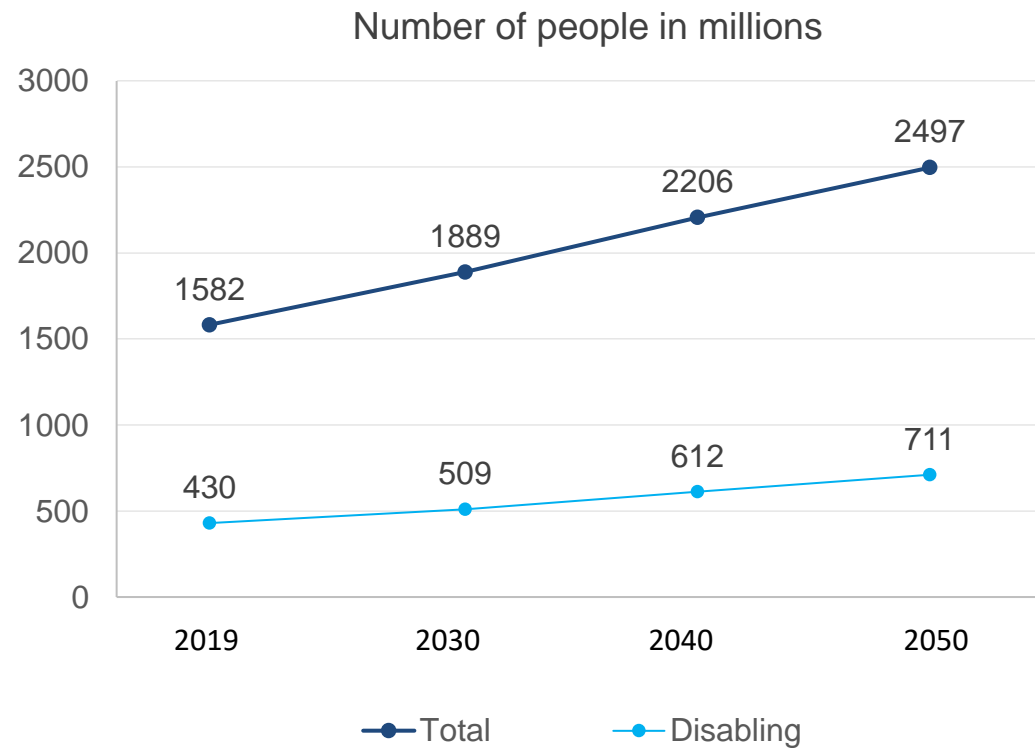
# A Franchise to Transform Lives & Connect People

**Our vision is to help people with inner ear hearing disorders to live life with unlimited connections**

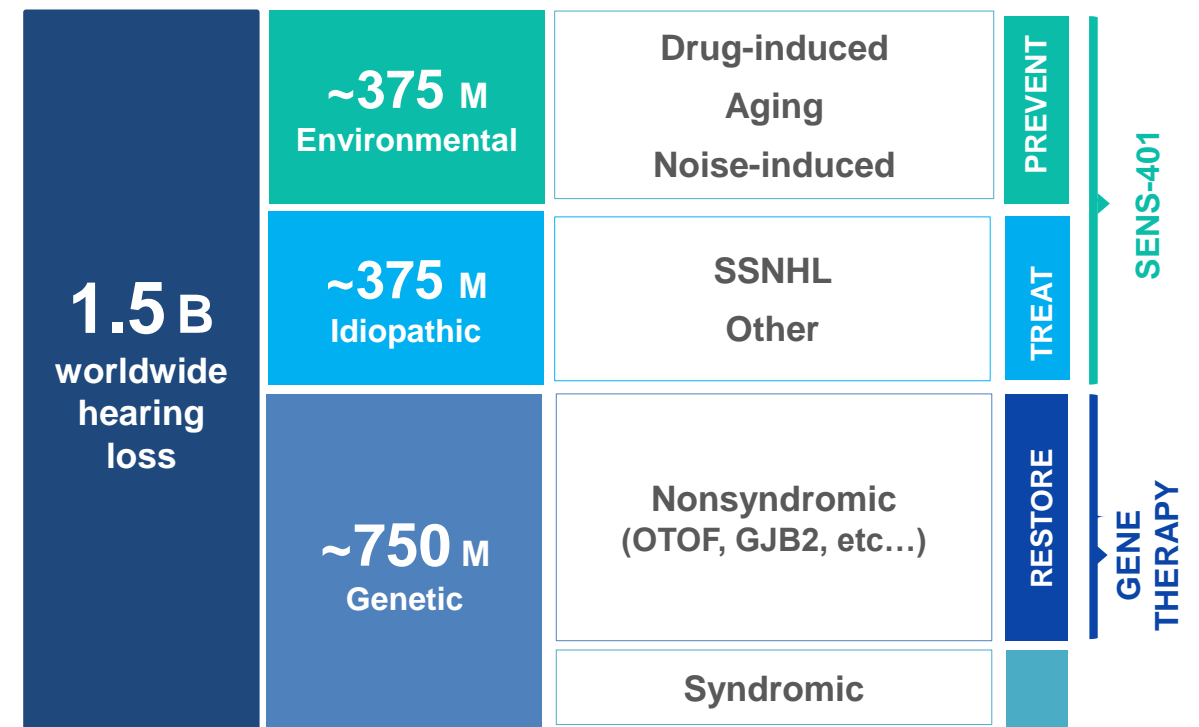


# Hearing Loss is a Massive Global Health Issue

Hearing loss is the most frequently occurring congenital sensory deficit, the largest modifiable risk factor for dementia and has a significant impact as people live longer.<sup>1-4</sup>



\*Chart adapted from World Report on Hearing. Geneva: World Health Organization; 2021.



Sources: Petit C et al., 2001, Snoeckx RL et al., 2005, Iizuka 2015 Human Molecular Genetics, World report on hearing. Geneva: World Health Organization; 2021

1. Amieva H et al., 2018; 2. Loughrey DG et al., 2018; 3. Hilgert N et al., 2008; 4. Livingston G et al. 2017

# SENS-401, Three Key Indications for Treatment and Prevention

**SENS-401 is a first-in-class drug aiming at treating or protecting against inner ear lesions that lead to sensory hair cell loss and nerve degeneration**

**SENS-401 demonstrated hearing loss and hair cell protection in different preclinical models**

**Protected by a solid intellectual property with two patent families.  
Orphan Drug Designation from EMA & FDA  
Pediatric Investigation Plan approved by EMA**

	Product	Indication	Discovery	<i>In vivo</i> POC	Preclinical	Phase 1	Phase 2	Phase 3	
PREVENT	SENS-401	Hearing preservation after cochlear implantation	[Progress bar]						
	SENS-401	Cisplatin Induced Ototoxicity	[Progress bar]						
TREAT	SENS-401	Sudden Sensorineural Hearing Loss	[Progress bar]						



# SENS-401 Has Enormous Potential and Enables our Franchise Vision



SENS-401 SSNHL clinical data and insight derisked further development of SENS-401 in other indications

SENS-401 CI preliminary data supports findings in SSNHL

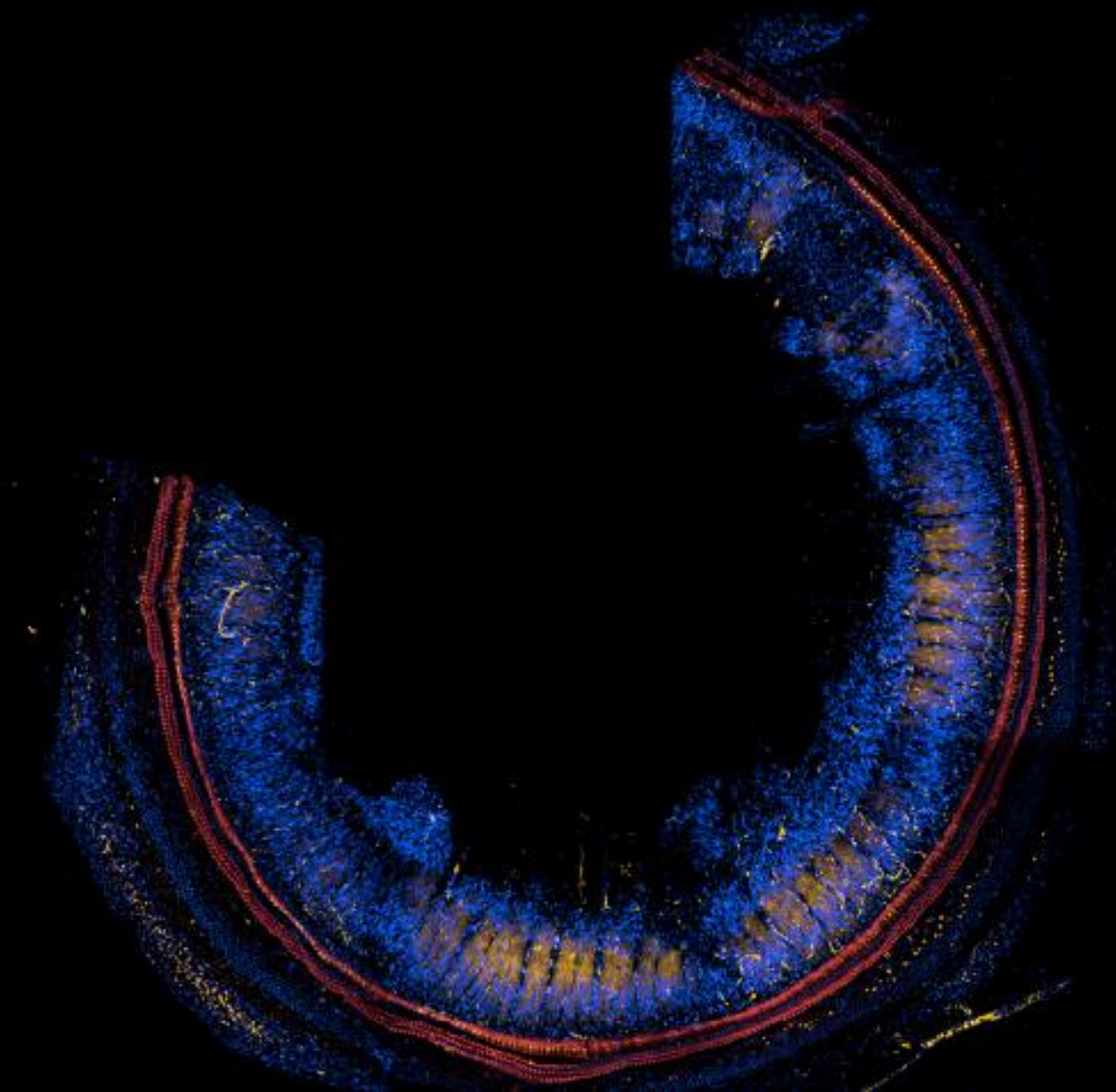




## THE IMPORTANCE OF RESIDUAL HEARING PRESERVATION

Professor Yann Nguyen  
ENT Surgeon  
Pitié Salpêtrière Hospital, Paris, France

July 5, 2023



# Conflict of Interest

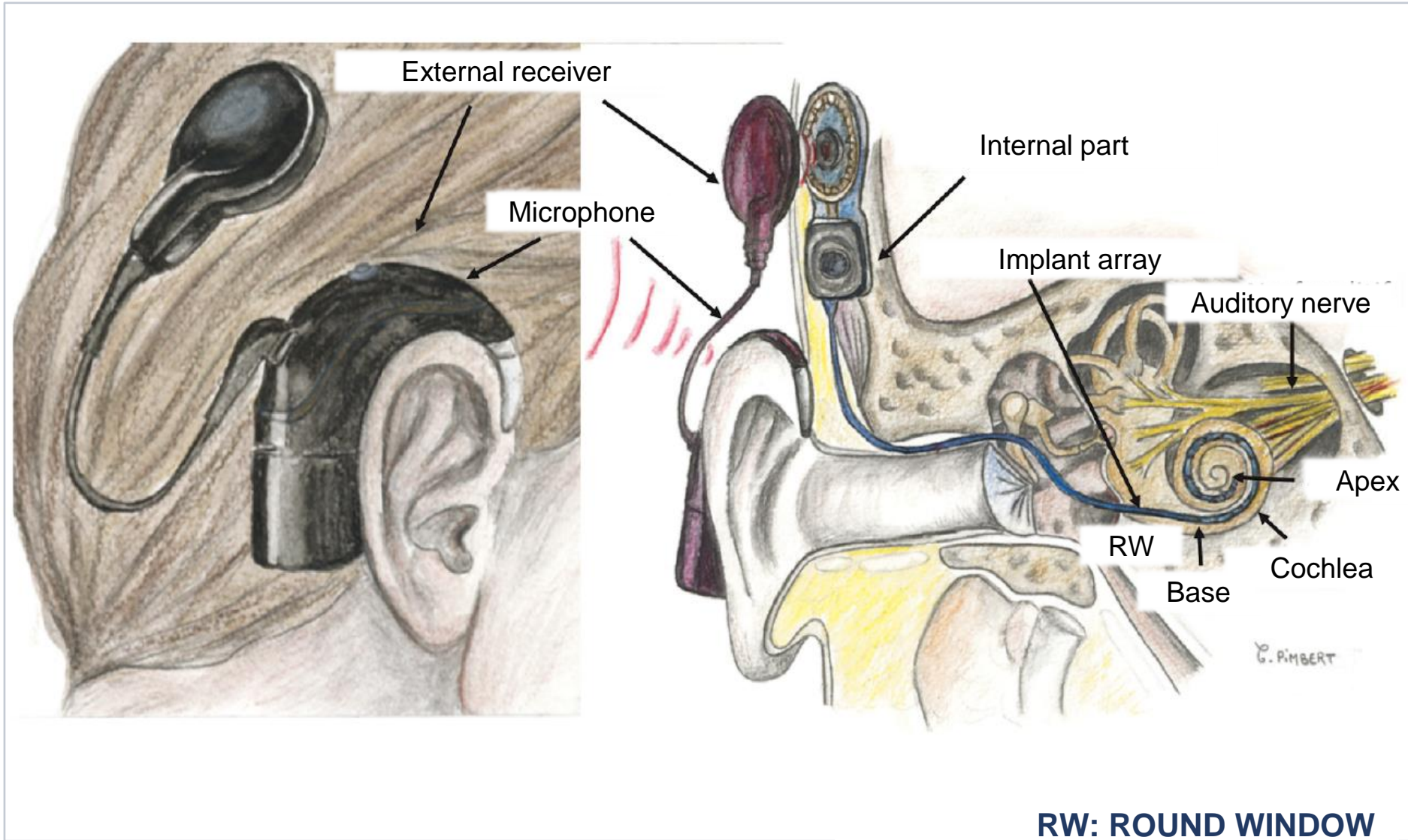
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**Laboratory and Medical department Research agreements:**  
Oticon Medical, Cochlear, MEDEL

**Consultant:**  
Collin Médical  
Sensorion  
Cilcare

**Principal investigator:**  
Sensorion's study of SENS-401 with cochlear implantation

# Cochlear Implantation (CI): a Remarkable Technology to Rehabilitate Severe to Profound Hearing Loss



**RW: ROUND WINDOW**  
ADAPTED FROM CÉLINE PIMBERT

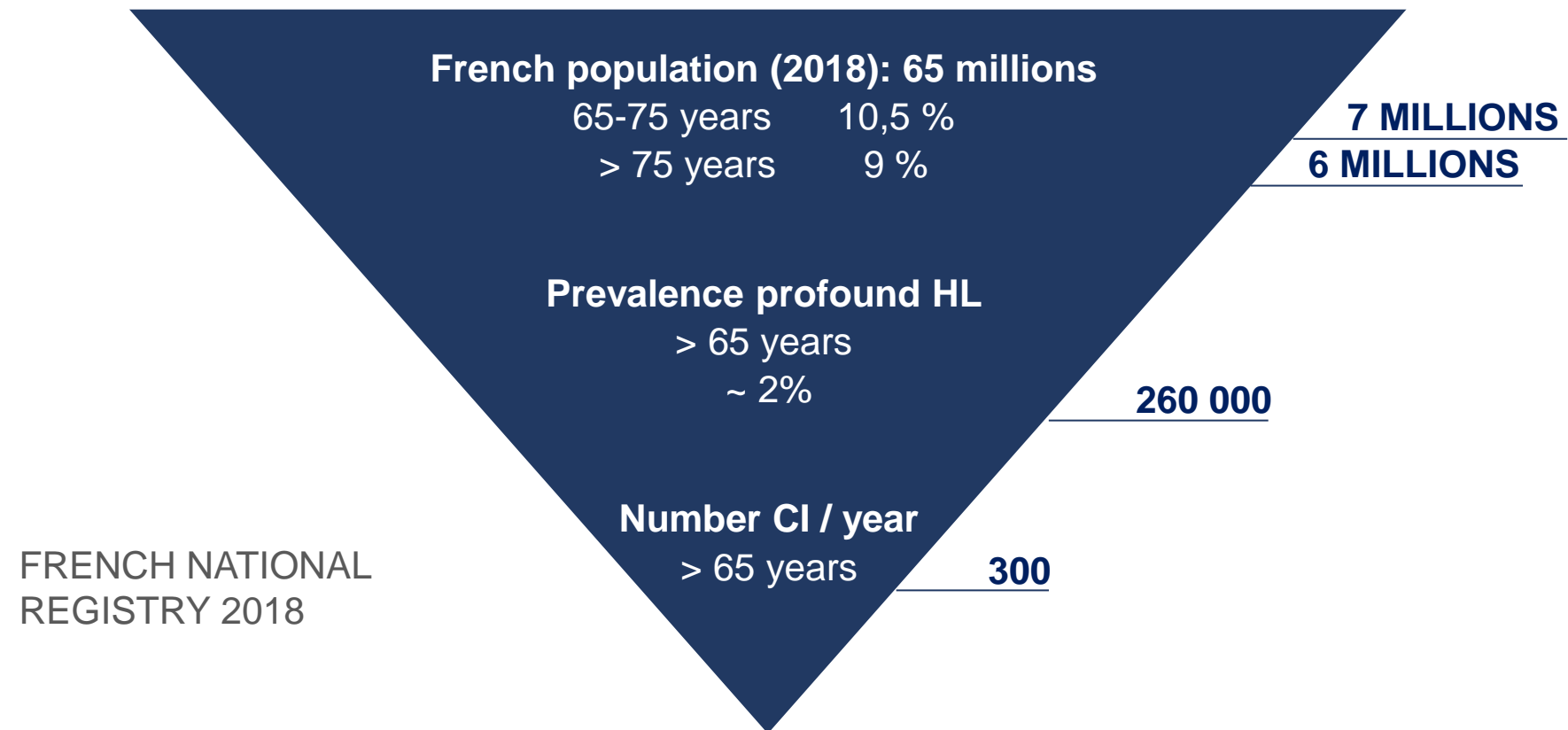


**COCHLEAR CI 632 DEVICE**  
(INTERNAL PART)

# Cochlear Implantation (CI): a Remarkable Technology to Rehabilitate Severe to Profound Hearing Loss

There are already one million patients in the world using cochlear implants but it would require many more to address the unmet medical need

Example from France  
But also true in all  
OECS countries

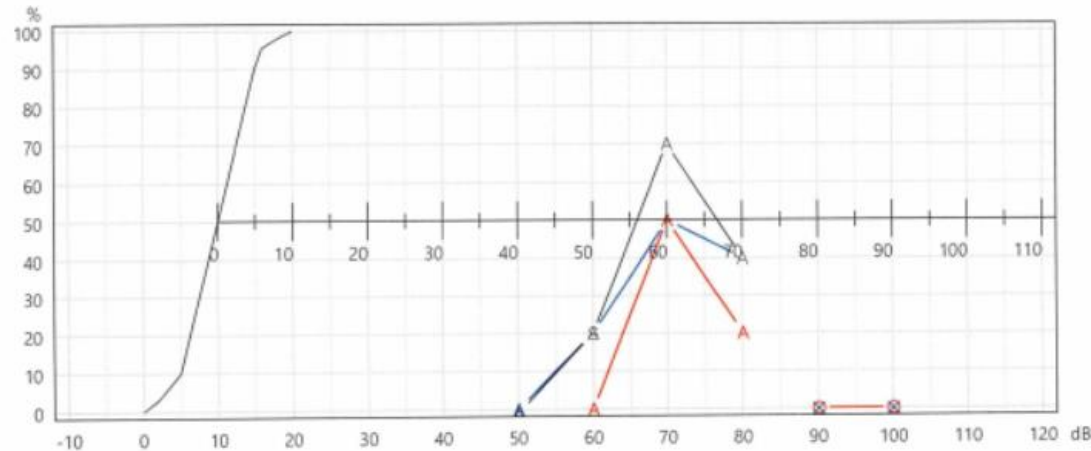
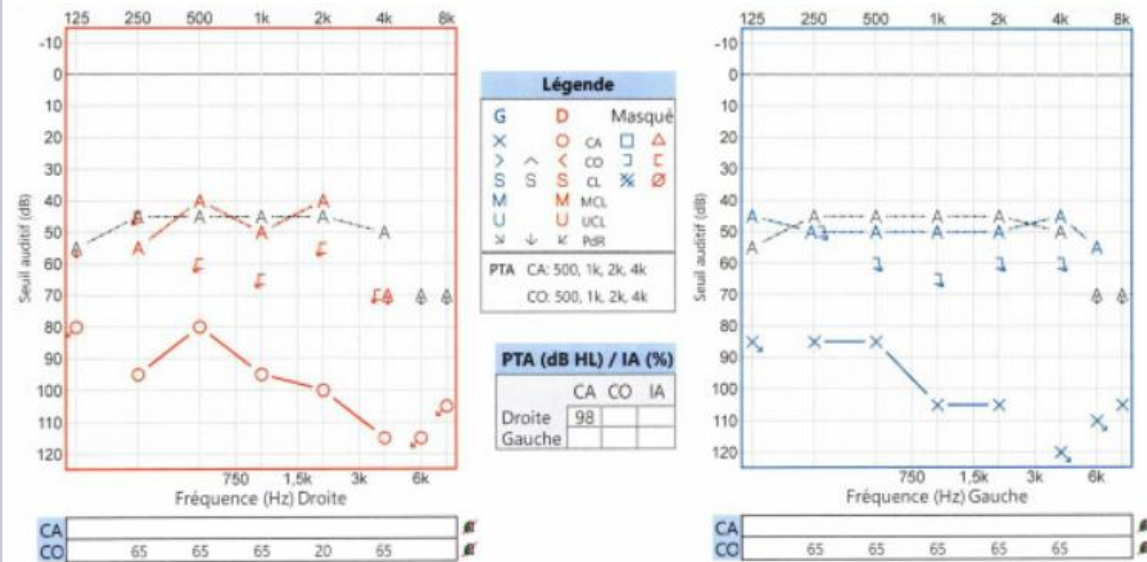


FRENCH NATIONAL  
REGISTRY 2018

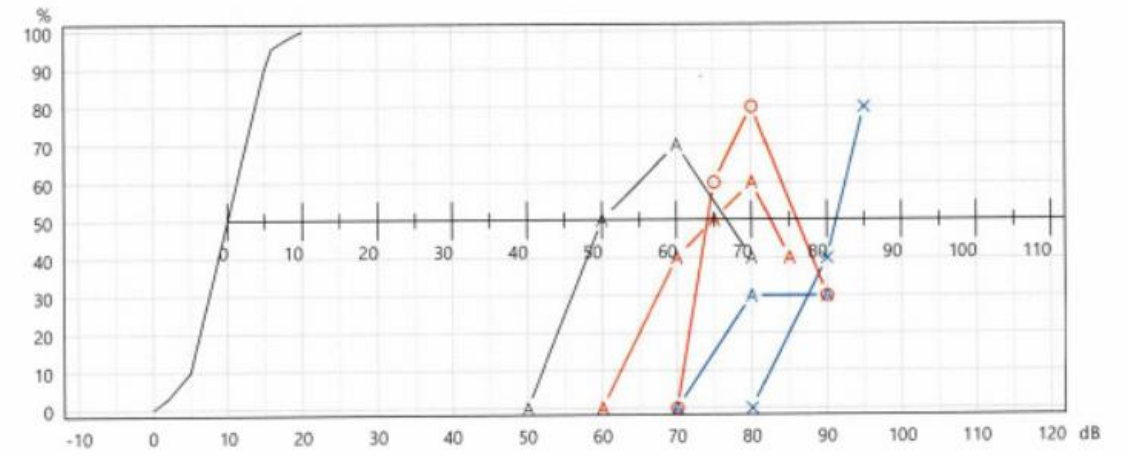
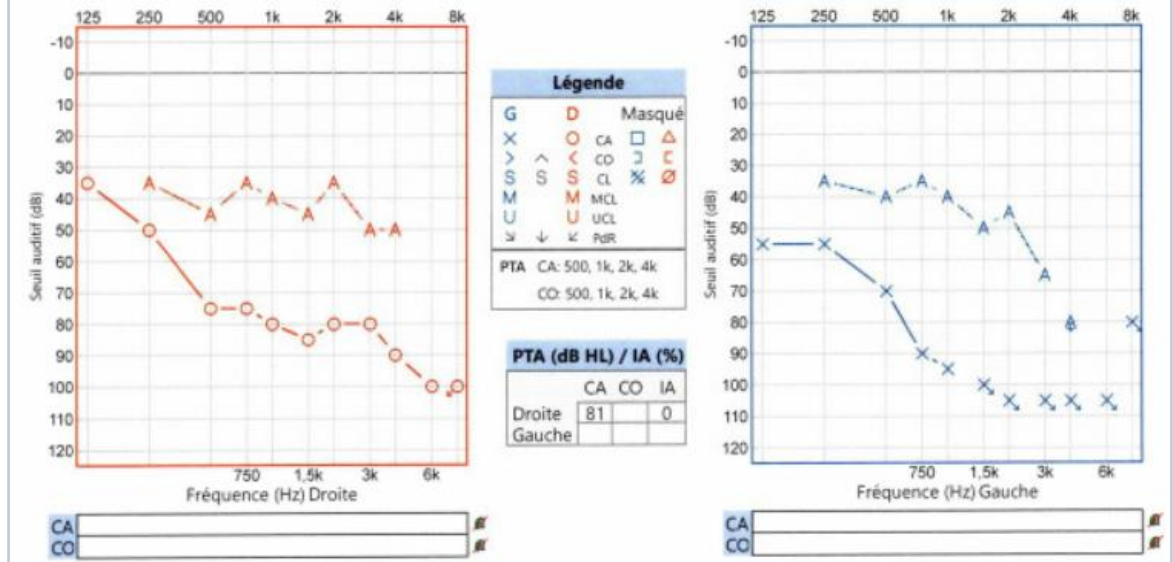
**< 2 % OF PROFOUNDLY DEAF PATIENTS  
> 65 YEARS ARE CI RECIPIENTS IN FRANCE**

# Residual Preoperative Hearing Varies among CI Candidates

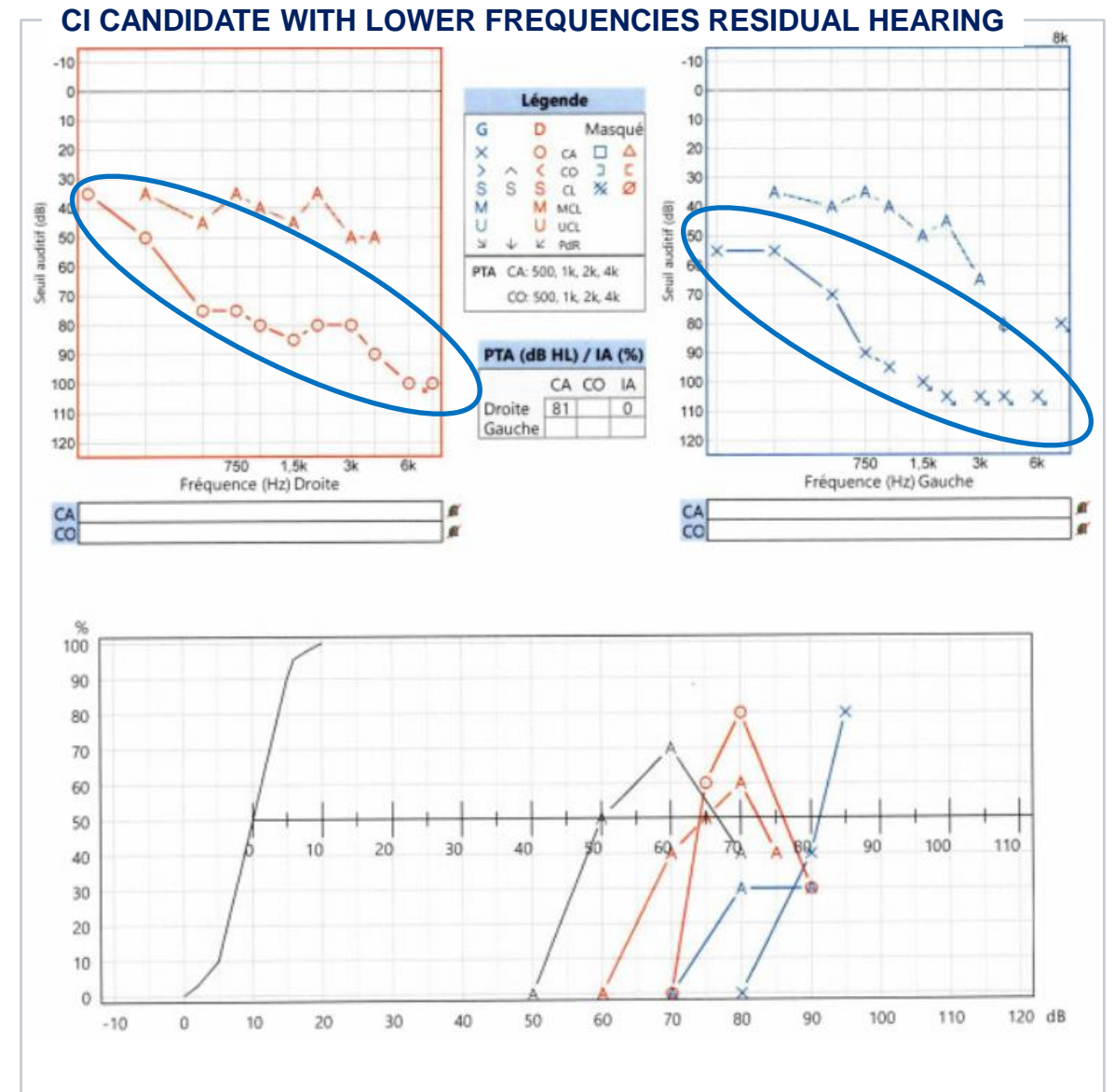
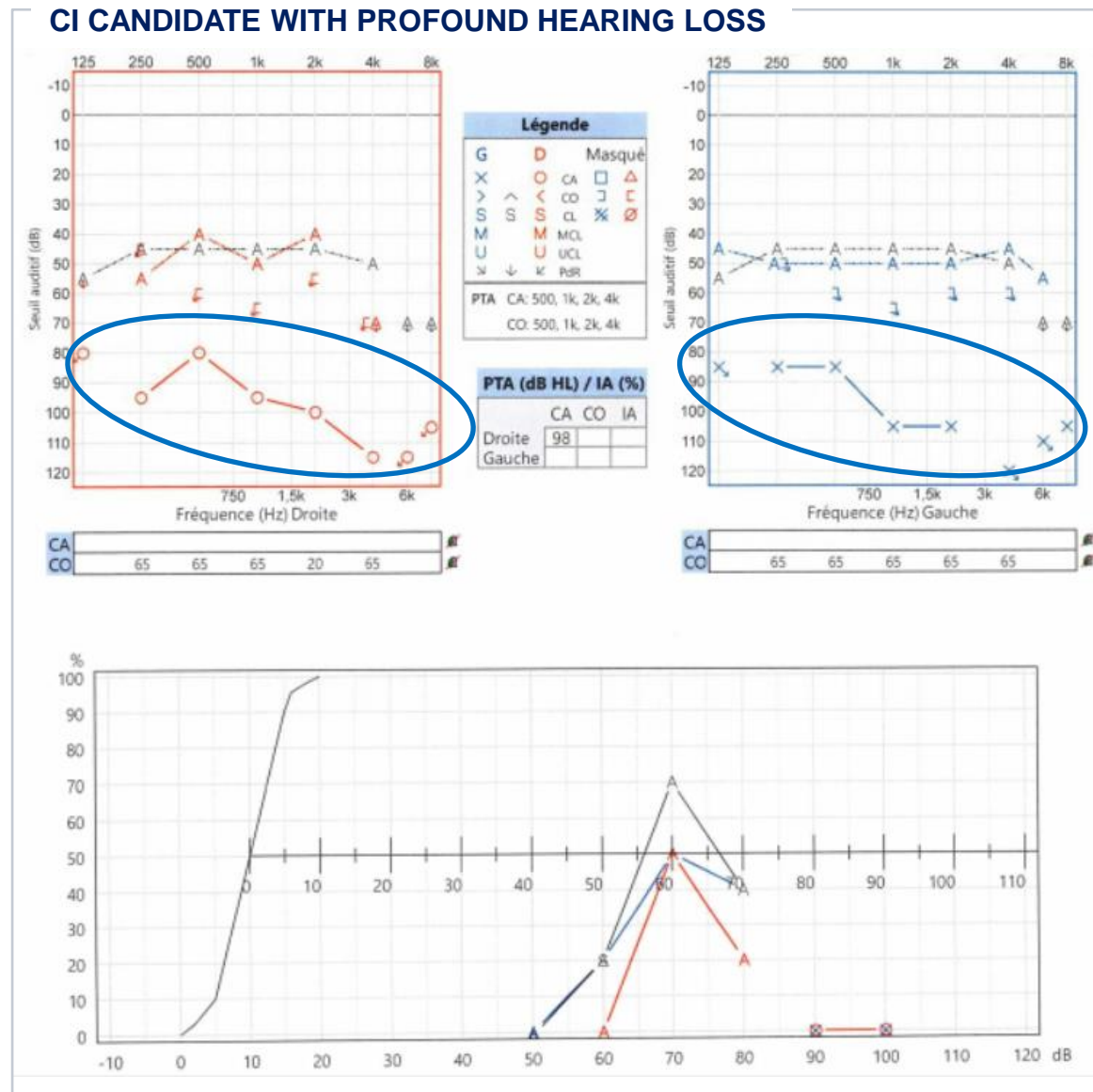
CI CANDIDATE WITH PROFOUND HEARING LOSS



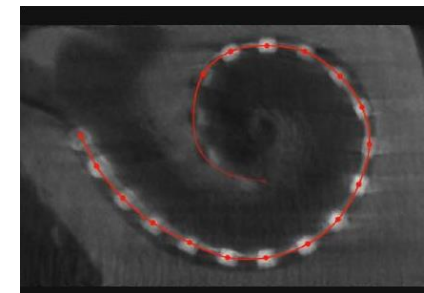
CI CANDIDATE WITH LOWER FREQUENCIES RESIDUAL HEARING



# Residual Preoperative Hearing Varies among CI Candidates



# Preserving Residual Hearing is Extremely Important

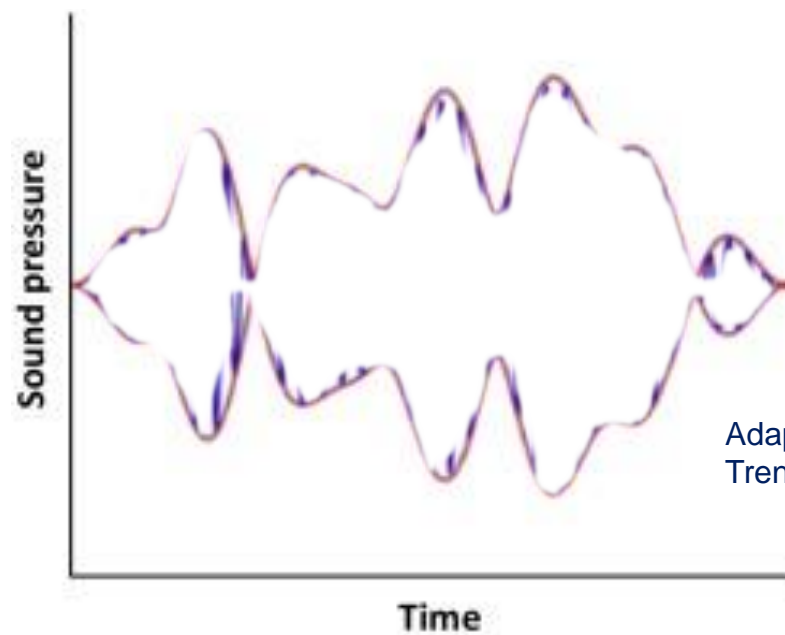


Conventional external processor (Cochlear®)

Electric stimulation only

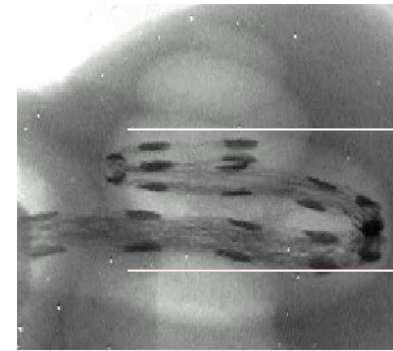
- Electric for full tonotopy

Loss of fine structure preservation



Adapted from Shannon R,  
Trend Cogn Sci, 2016

# Preserving Residual Hearing is Extremely Important



Acoustic stimulation

Electric stimulation

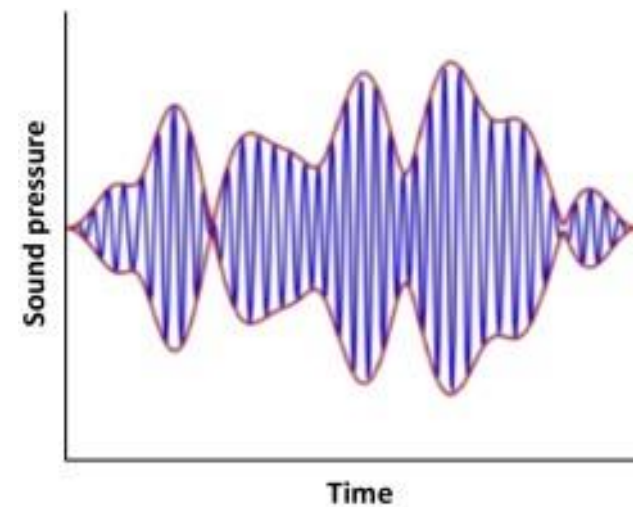


Hybrid electro-acoustic stimulator (Cochlear®)

Hybrid Electro-acoustic stimulation

- Acoustic for lower frequencies
- Electric for higher frequencies

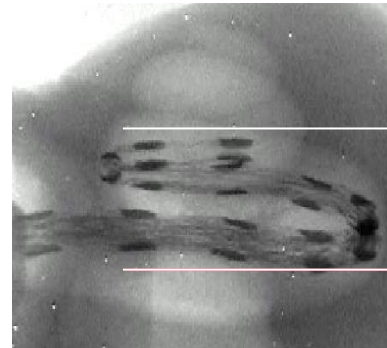
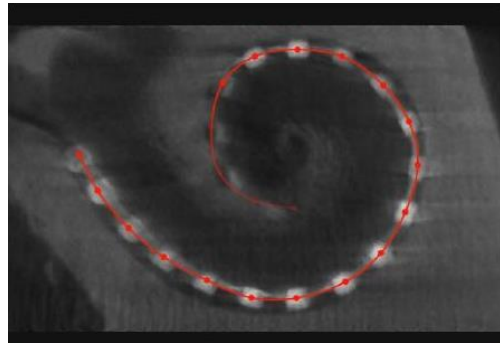
Lower frequencies  
fine structure preservation



Adapted from Shannon R,  
Trend Cogn Sci, 2016



# Preserving Residual Hearing is Extremely Important



Acoustic stimulation

Electric stimulation

Hybrid Electro-acoustic stimulation

- Acoustic for lower frequencies
- Electric for higher frequencies

Lower frequencies fine structure preservation

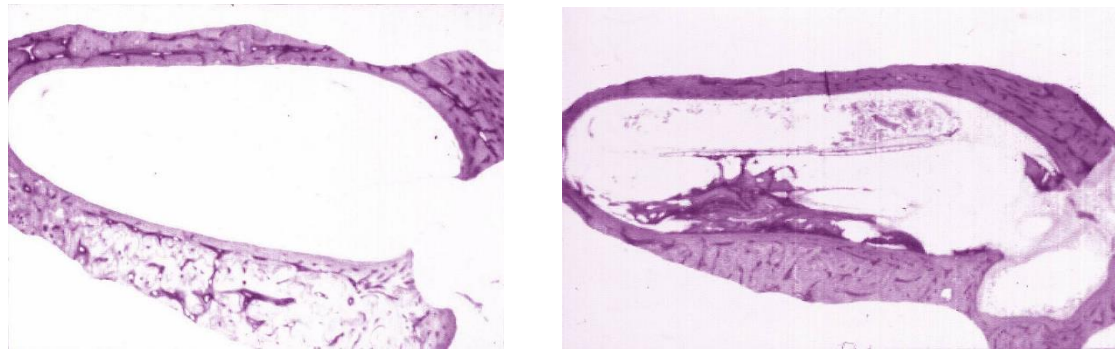
- Better speech in noise
  - Better music perception
- (Based on 21 studies, Schaeffer et al, Int J Audiol 2021)

**“EVEN THOUGH MY HEARING IS NOT USEFUL TO COMMUNICATE ANYMORE, I AM AFRAID TO LOSE IT”**

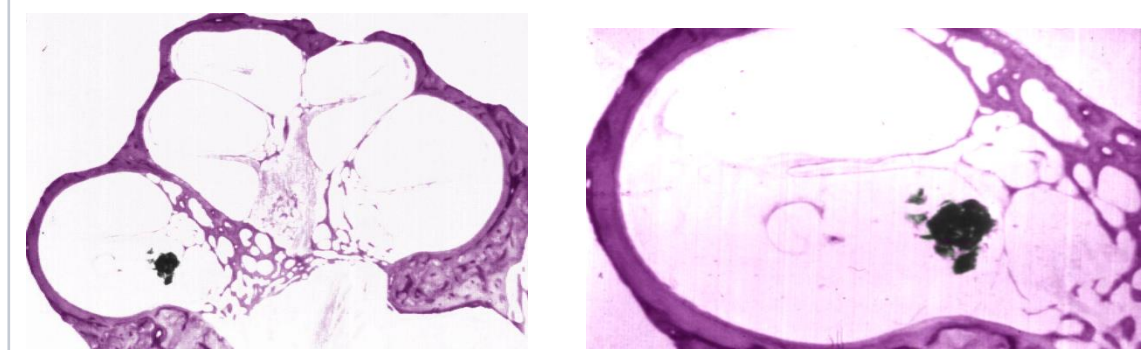
# Various Mechanisms Result in Residual Hearing Loss

- Mechanical disruption of intracochlear structures (basilar membrane, spiral ligament, modiolar wall, spiral osseous lamina)
- Inflammatory process (fibrosis in perilymphatic space) and secondary apoptosis
- Disturbance of fluid balance (endolymphatic or perilymphatic)
- Acute or chronic bacterial infection
- Cochlear mechanism dysfunction

**MECHANICAL DISRUPTION  
OF INTRACOCHELEAR STRUCTURES**



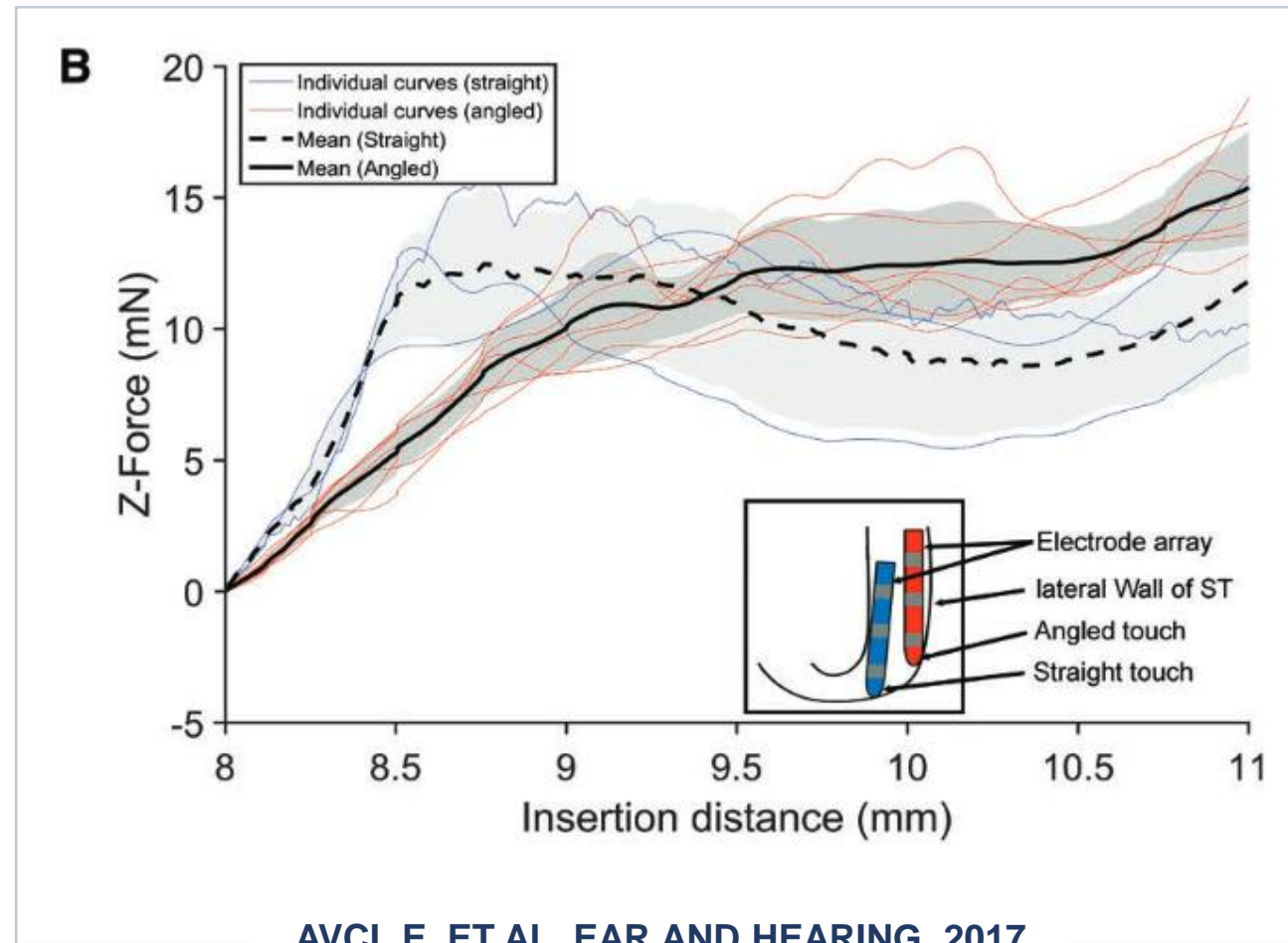
**INFLAMMATORY PROCESS AND  
SECONDARY APOPTOSIS**



# Several Factors Influence Array Insertion Trauma

## Cochlear Anatomy

- **Cochlear anatomy**
- Array diameter
- Array stiffness
- Manual vs robot-based insertion
- Drug administration

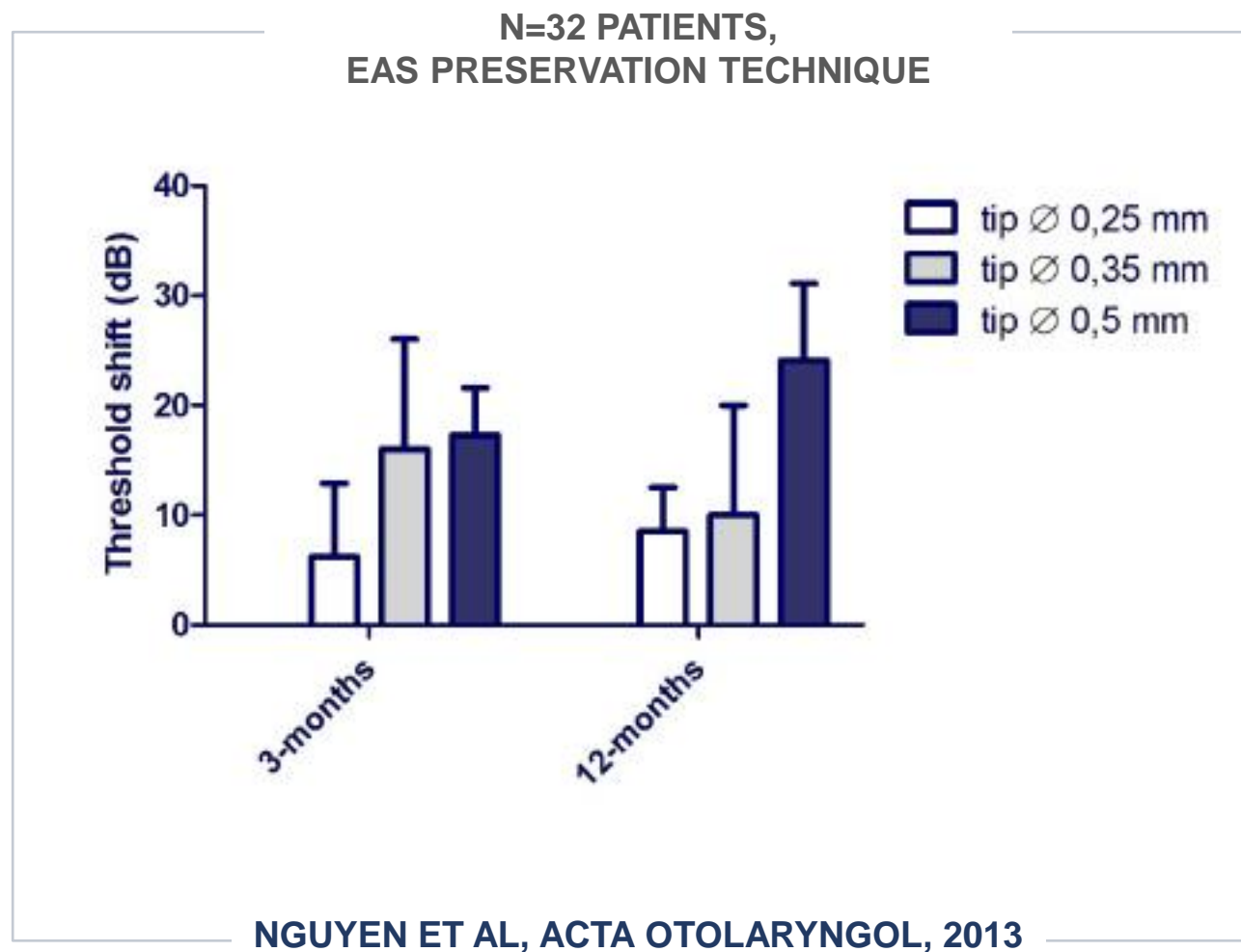


AVCI, E. ET AL, EAR AND HEARING, 2017

# Several Factors Influence Array Insertion Trauma

## Array Diameter

- Cochlear anatomy
- **Array diameter**
- Array stiffness
- Manual vs robot-based insertion
- Drug administration

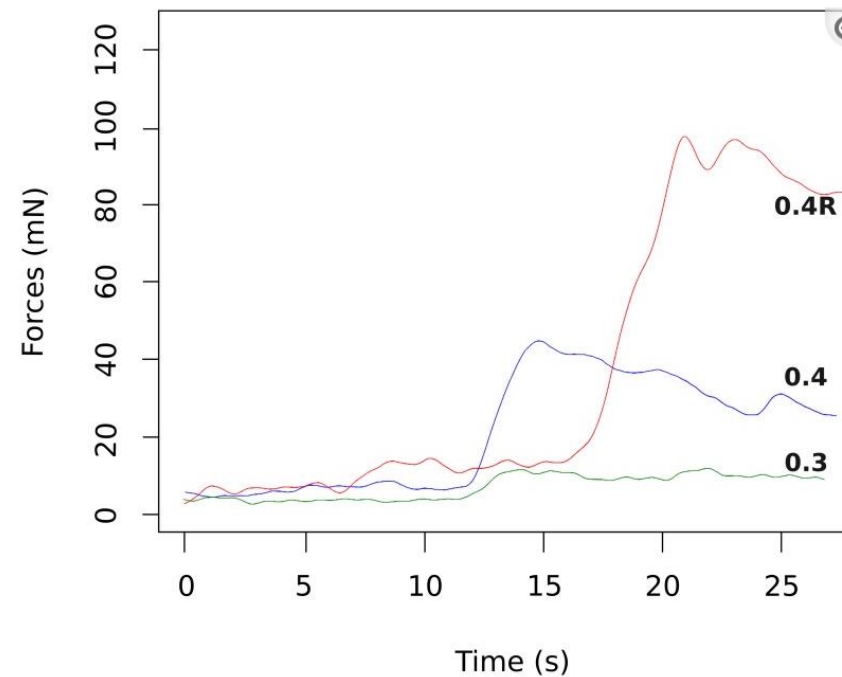


# Several Factors Influence Array Insertion Trauma

## Array Stiffness

- Cochlear anatomy
- Array diameter
- **Array stiffness**
- Manual vs robot-based insertion
- Drug administration

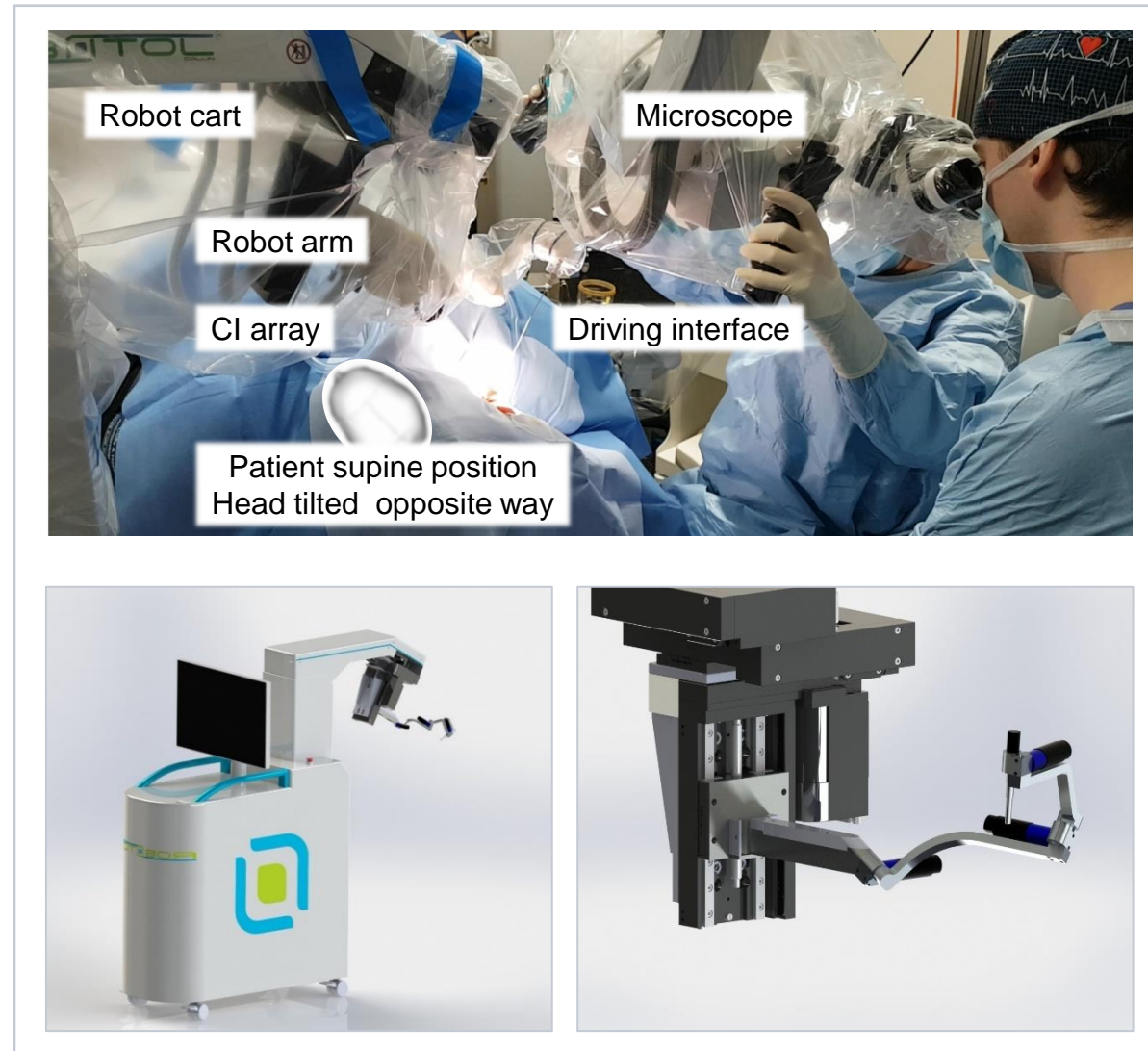
FRICITION FORCES WITH A 0.3, 0.4 SOFT, OR 0.4 HARD ARRAY DIAMETER



DROUILLARD ET AL, PLOS ONE, 2017

# Insertion Mechanism Influences Insertion Trauma

- Cochlear anatomy
- Array diameter
- Array stiffness
- **Manual vs robot-based insertion**
- Drug administration



# Several Factors Influence Array Insertion Trauma

## Corticosteroids Have a Limited Effect

- Cochlear anatomy
- Array diameter
- Array stiffness
- Manual vs robot-based insertion
- **Drug administration**

Clinical Trial > Laryngoscope. 2012 Jan;122(1):190-5. doi: 10.1002/lary.22142.

### The role of preoperative, intratympanic glucocorticoids for hearing preservation in cochlear implantation: a prospective clinical study

Gunesh P Rajan<sup>1</sup>, Jafri Kuthubutheen, Naveen Hedne, Jay Krishnaswamy

Affiliations + expand

PMID: 22183635 DOI: 10.1002/lary.22142

> Otol Neurotol. 2015 Sep;36(9):1480-5. doi: 10.1097/MAO.0000000000000847.

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

Alex D Sweeney<sup>1</sup>, Matthew L Carlson, M Geraldine Zuniga, Marc L Bennett, George B Wanna, David S Haynes, Alejandro Rivas

Affiliations + expand

PMID: 26375969 DOI: 10.1097/MAO.0000000000000847

Randomized Controlled Trial > Audiol Neurotol. 2017;22(4-5):292-302. doi: 10.1159/000485310. Epub 2018 Jan 13.

### The Role of Preoperative Steroids for Hearing Preservation Cochlear Implantation: Results of a Randomized Controlled Trial

Jafri Kuthubutheen<sup>1</sup>, Samidha Joglekar, Leah Smith, Lendra Friesen, Kari Smilsky, Tara Millman, Amy Ng, David Shipp, Harvey Coates, Christoph Arnoldner, Julian Nedzelski, Joseph Chen, Vincent Lin

Affiliations + expand

PMID: 29332068 DOI: 10.1159/000485310

Randomized Controlled Trial > Hear Res. 2021 May;404:108224. doi: 10.1016/j.heares.2021.108224. Epub 2021 Feb 28.

### Systemic methylprednisolone for hearing preservation during cochlear implant surgery: A double blinded placebo-controlled trial

Stephen J O'Leary<sup>1</sup>, June Choi<sup>2</sup>, Karina Brady<sup>3</sup>, Sheila Matthews<sup>3</sup>, Katie Boncza Ozdowska<sup>3</sup>, Matthew Payne<sup>3</sup>, Tim McLean<sup>3</sup>, Alex Rousset<sup>3</sup>, Jonathon Lo<sup>3</sup>, Nathan Creber<sup>3</sup>, Sylvia Tari<sup>3</sup>, Richard Dowell<sup>4</sup>, Robert Briggs<sup>5</sup>

Affiliations + expand

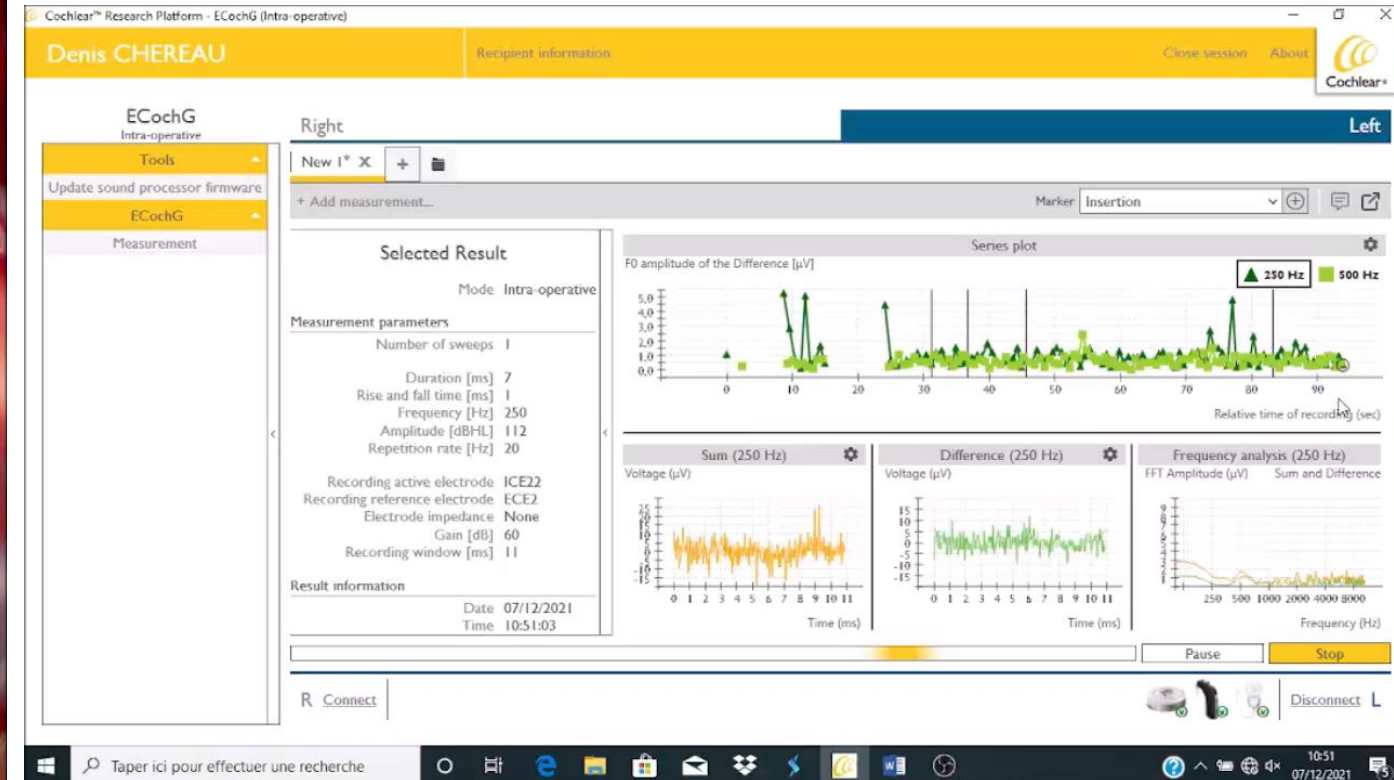
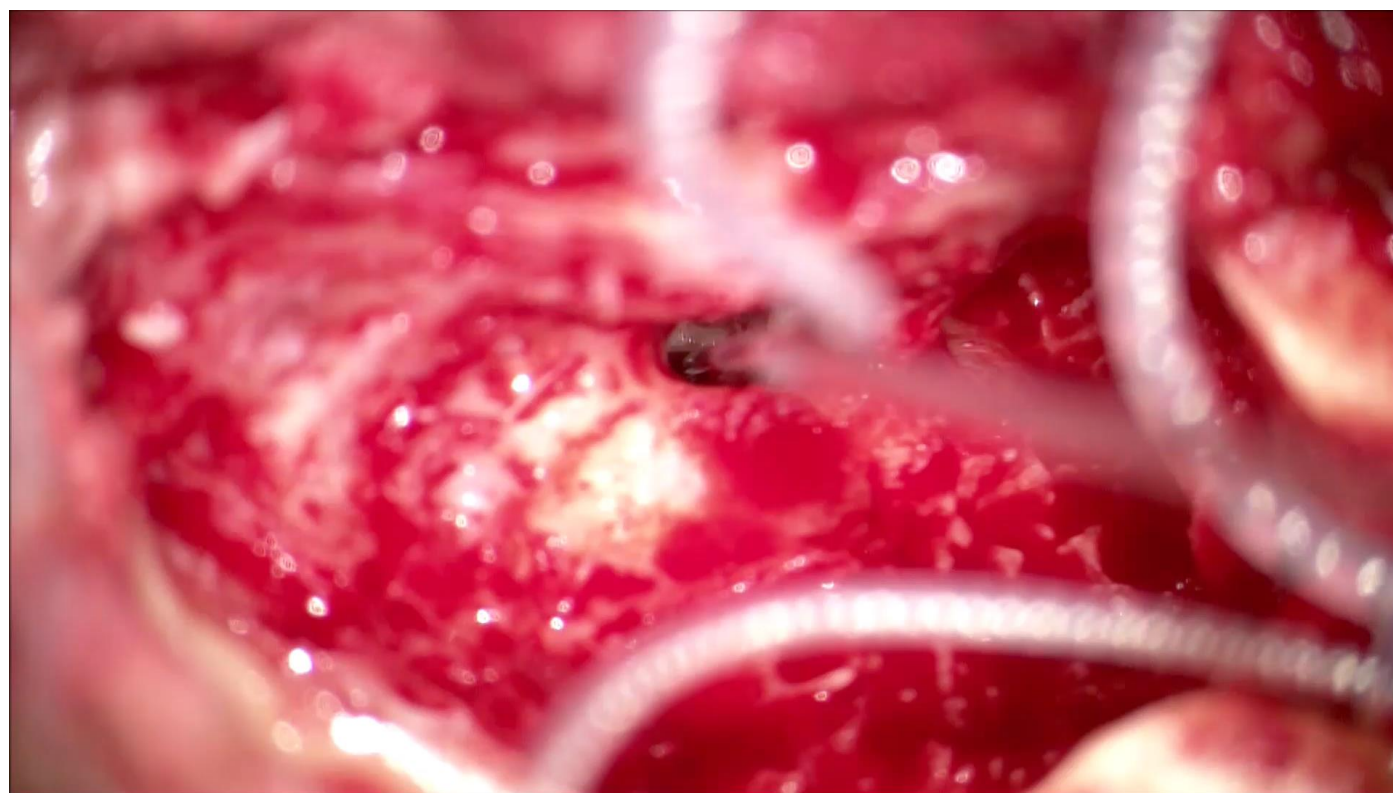
PMID: 33774594 DOI: 10.1016/j.heares.2021.108224

**“OVERALL, EVIDENCE OF ANTI-INFLAMMATORY EFFECTS IN HUMANS IS STILL SCARCE”**

Parys QA, et al. Inner Ear Pharmacotherapy for Residual Hearing Preservation in Cochlear Implant Surgery: A Systematic Review. Biomolecules. 2022

# Cochlear Implant Surgical Standard Technique

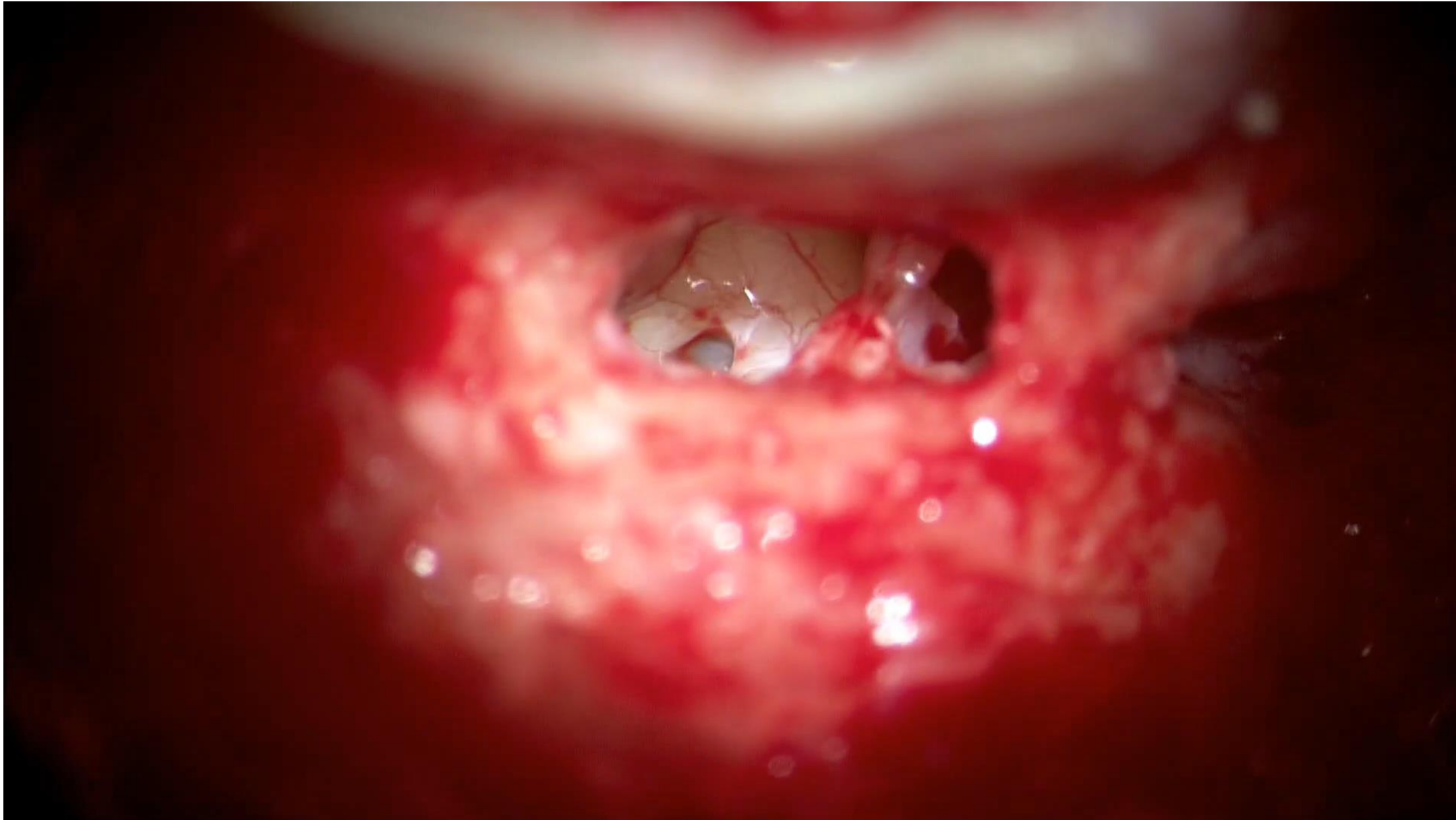
- ECoChG monitoring provides information on the chances of preserving residual hearing during the surgical procedure
- The signal can be obtained if the hearing threshold < 80 dB at 500 Hz
- It can guide the robot-based implant insertion to preserve residual hearing



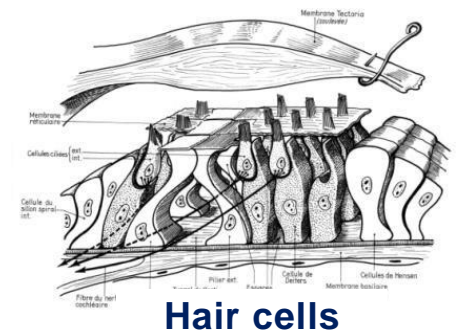
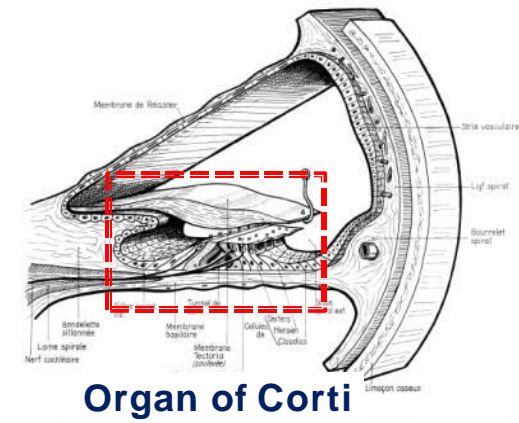
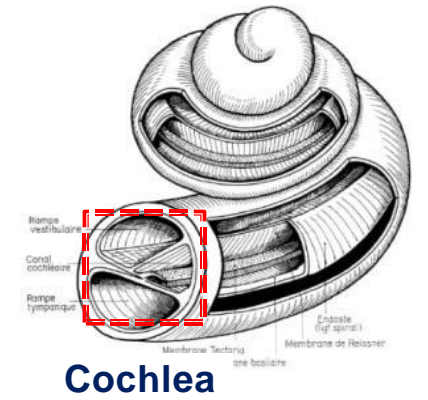
(Dr Isabelle Mosnier, AP-HP; Mathilde Cosnard, Cochlear France)



# Cochlear Implant Surgical Standard Technique



# Perilymph Sampling Protocol



With the courtesy of Prof Steven O'Leary

# Perilymph Sampling Protocol



AP-HP Sorbonne Université

INSTITUT PASTEUR

Inserm

## Implant cochléaire Insertion du porte-électrodes

AP-HP6, GH Pitié-Salpêtrière, Service ORL  
Unité Fonctionnelles Implants Auditifs et explorations fonctionnelles  
Centre référent « Implants cochléaire et du tronc cérébral de l'adulte en Île-de-France »  
Centre Maladies rares « Surdit   g  n  tique de l'adulte » et « Neurofibromatose de type 2 »  
Centre de Recherche Clinique en Audiologie Adulte  
Sorbonne Universit    
Institut Pasteur / Inserm, Institut de l'audition, Technologie et th  rapie g  n  tique de la surdit  

# A New Drug for Hearing Preservation during Cochlear Implantation Could Be Extremely Valuable

1. **Residual hearing preservation** in implanted patients **improves hearing performance and quality of life**
2. Cochlear implantation criteria could be further expanded if residual hearing preservation rate are higher
3. **Array design improvement, atraumatic insertion and drug otoprotection** are key to improving hearing preservation
4. Although **corticosteroids are widely used** in current practice, there are **no guidelines** for doses and delivery route

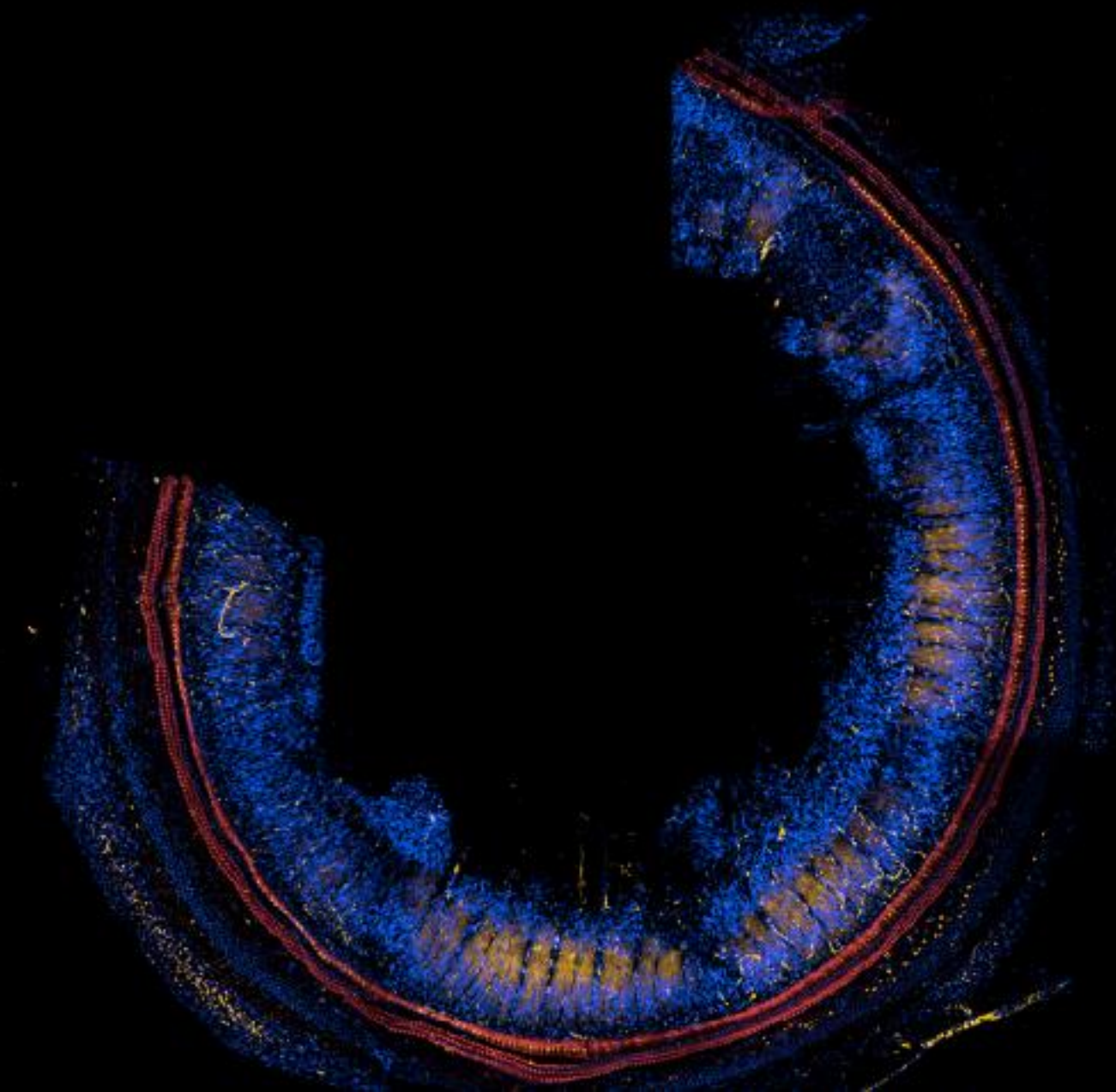
▶ **A more efficient and reliable drug is needed by the medical community**



## **PHASE 2A STUDY KEY PRELIMINARY RESULTS**

Dr. Géraldine Honnet  
Chief Medical Officer  
Sensorion

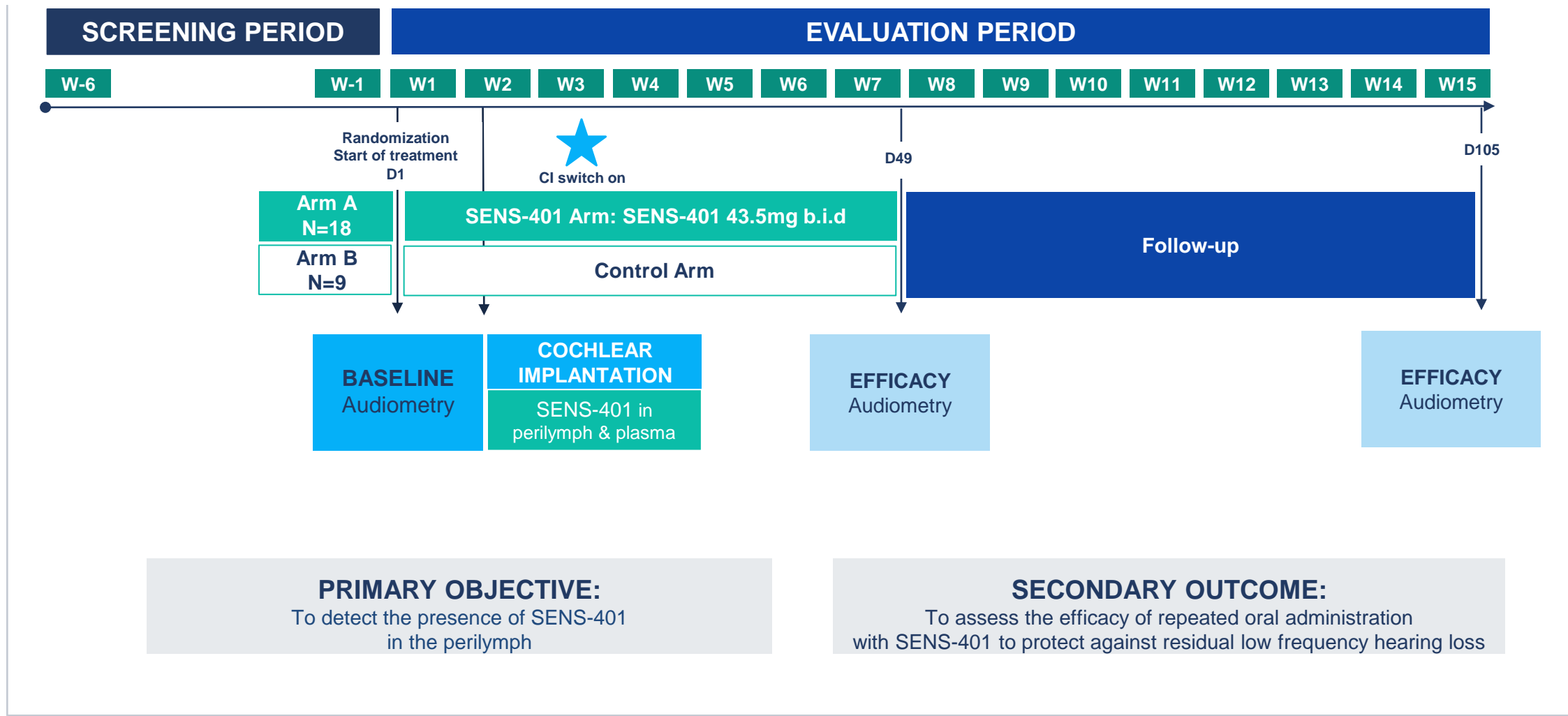
July 5, 2023



# Study Design



A Phase 2a, Multicenter, Randomized, Controlled, Open-label Study to Evaluate the Presence of SENS-401 in the Perilymph after 7 days of Repeated Oral Administration in Adult Participants Scheduled for Cochlear Implantation





1

**BASELINE  
CHARACTERISTICS  
& SAFETY**



# Patient Baseline Characteristics are Comparable between the Two Groups

Number of patients		Control arm (N=4)	SENS-401 arm (N=5)	Total (N=9)
<b>Age (years)</b>		72	66	69
<b>Gender</b>	Female	2	4	6
	Male	2	1	3
<b>PTA (dB HL)</b>	Mean of 250, 500 and 750 Hz	70	66	68
	500 Hz	66	69	68
<b>Cause of hearing loss</b>	Congenital non-inherited		1	1
	Disease-related hearing loss	1		1
	Infection		1	1
	Inherited	1	2	3
	Trauma	1		1
	Unknown cause	1	1	2



# SENS-401 Confirms a Good Safety Profile

SEVERITY	STUDY DRUG CAUSALITY				
	Related		Not related	TOTAL	
Mild	Constipation	3	Vomiting	1	
	Myalgia	1	Laryngitis	1	
	Dysgeusia	1	Hypokalemia	1	
	Nausea	1	Dizziness	1	
	<b>Total</b>	<b>6</b>		<b>4</b>	<b>10</b>
Moderate			Left ear pain	1	
			Headache	1	
			Constipation	1	
<b>Total</b>	<b>0</b>		<b>3</b>	<b>3</b>	
Severe			Acute Vertigo	1	
<b>Total</b>	<b>0</b>		<b>1</b>	<b>1</b>	
<b>TOTAL</b>		<b>6</b>		<b>8</b>	<b>14</b>

- Despite being administered for an unprecedented duration of 7 weeks, SENS-401 maintained a good safety profile at an oral dose level of 43.5 mg, administered twice daily (b.i.d.)
- This aligns with previous findings at the same daily dosage level, confirming good safety profile for the study drug

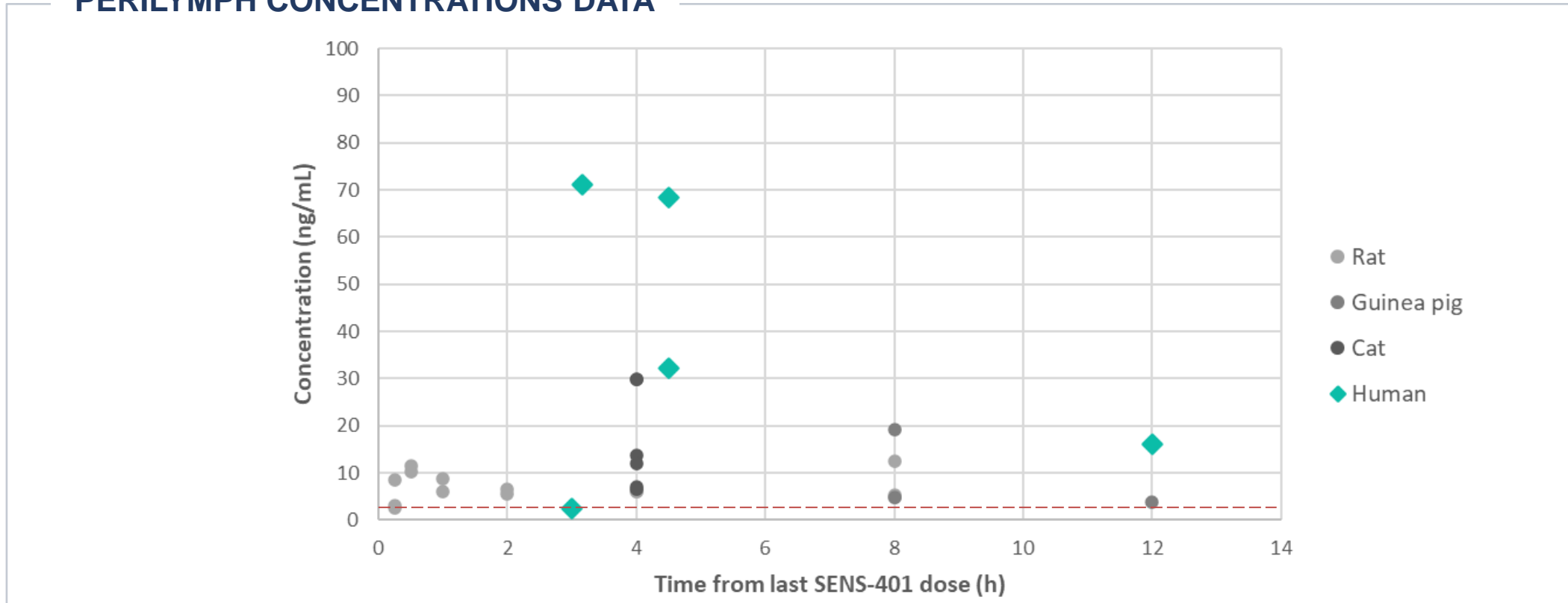
2

**PRIMARY  
OBJECTIVE**



# SENS-401 is Detected in the Perilymph of the First 5 Treated Patients at Levels Consistent with Those Observed in Animals

## PERILYMPH CONCENTRATIONS DATA



--- Minimal perilymph concentration in animals

- Plasma concentrations of SENS-401 in humans at steady state: dosing of 43.5 mg b.i.d range from 20-90 ng/mL
- Perilymph concentrations in animal models at equivalent plasma levels range from 2 to 30 ng/mL
- The observed values in the first 5 patients are in line with the predicted values, ranging from 2 to 70 ng/mL

2

**SECONDARY  
OBJECTIVES**



# Residual Low Frequency Hearing Benefits for Cochlear Implant Users

- 80% of cochlear implant candidates now have bilateral low-frequency residual hearing before surgery.<sup>1</sup>
- Many cochlear implant candidates fear losing their residual hearing, as this may occur in as many as 50 - 70% of CI surgeries.<sup>2</sup>



Improved speech perception  
in quiet and in noise <sup>3,4</sup>



Improved music perception <sup>5-7</sup>



More natural sound quality <sup>5</sup>



Improved localization <sup>8</sup>

1. Sheffield SW, et al. J Am Acad Audiol. 2015 Feb;26(2):145-54.  
2. Wijewickrema S, et al. PLoS One. 2022 Jul 14;17(7):e0269187.  
3. Adunka OF, et al. Laryngoscope. 2013 Oct;123(10):2509-15.

4. Park LR, et al. Ear Hear. 2019 Jul/Aug;40(4):849-857.  
5. Kelsall DC, et al. Otol Neurotol. 2017 Oct;38(9):1251-1261.  
6. Parkinson AJ, et al. Otol Neurotol. 2019 Mar;40(3):e283-e289.

7. Gfeller KE, et al. Audiol Neurotol. 2006;11 Suppl 1:12-5.  
8. Härkönen K, et al. Eur Arch Otorhinolaryngol. 2017 Oct;274(10):3599-3604.

# Residual Low Frequency Hearing Benefits for Cochlear Implant Users

**Initial shift\***  
(2-4 weeks postoperative)  
between surgery and initial activation of the device

- **Attributed to perioperative factors**

**Second shift\***  
(3-6 months postoperative)

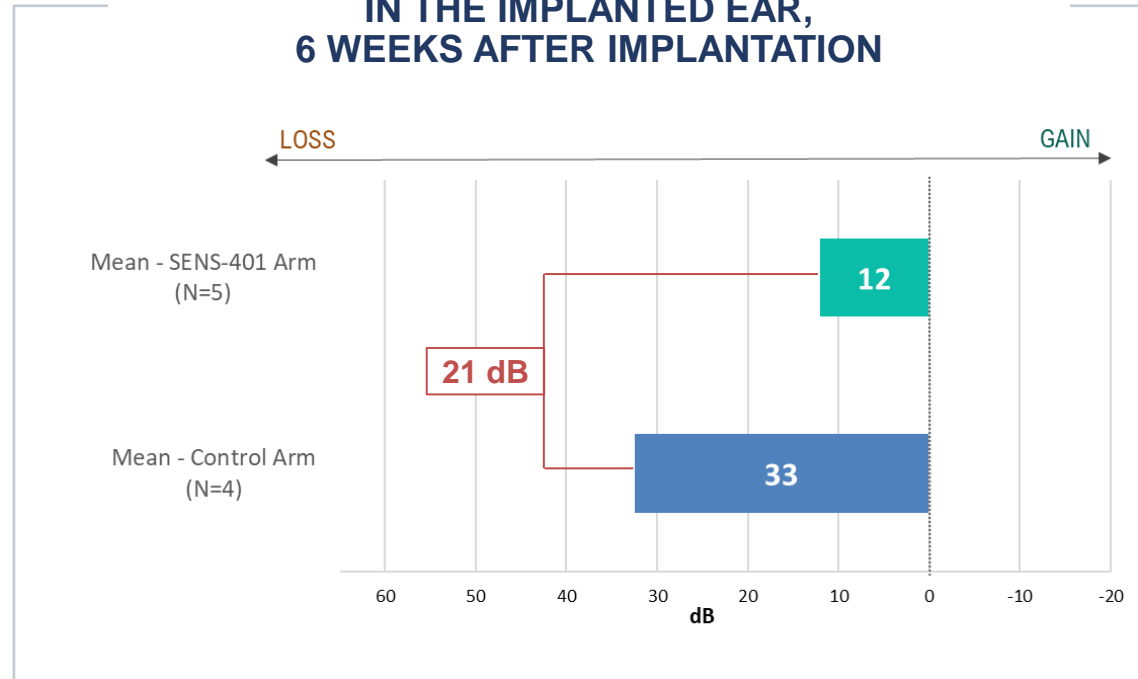
- **Attributed to intracochlear fibrosis, excitotoxic changes from electrical and acoustic stimulation**

**Postoperative hearing preservation** defined as:  
unaided air-conduction **thresholds < 85 dB** at 125, 250, and 500 Hz

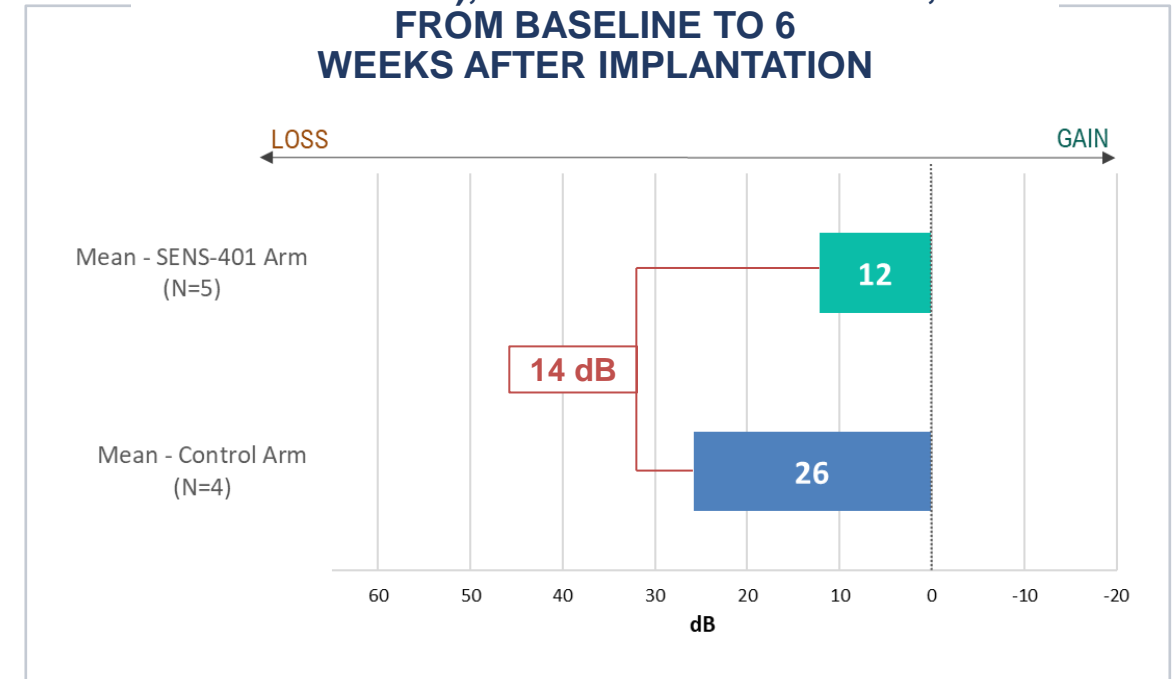
*\*Jensen et al., Hearing Preservation After Cochlear Implantation, 2021*

# SENS-401 Preserves Early Loss of Residual Hearing - As Shown in all Five Patients Treated so far

MEAN CHANGE FROM BASELINE AT 500 HZ,  
IN THE IMPLANTED EAR,  
6 WEEKS AFTER IMPLANTATION



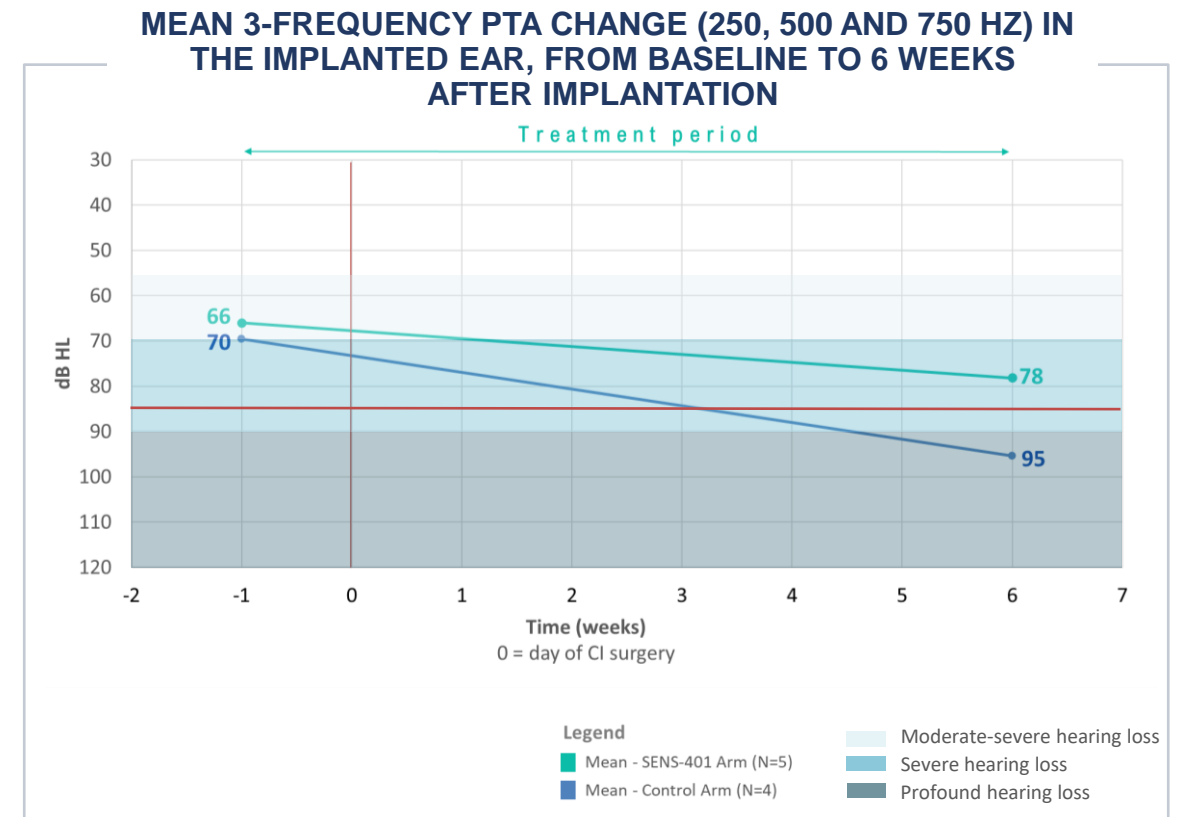
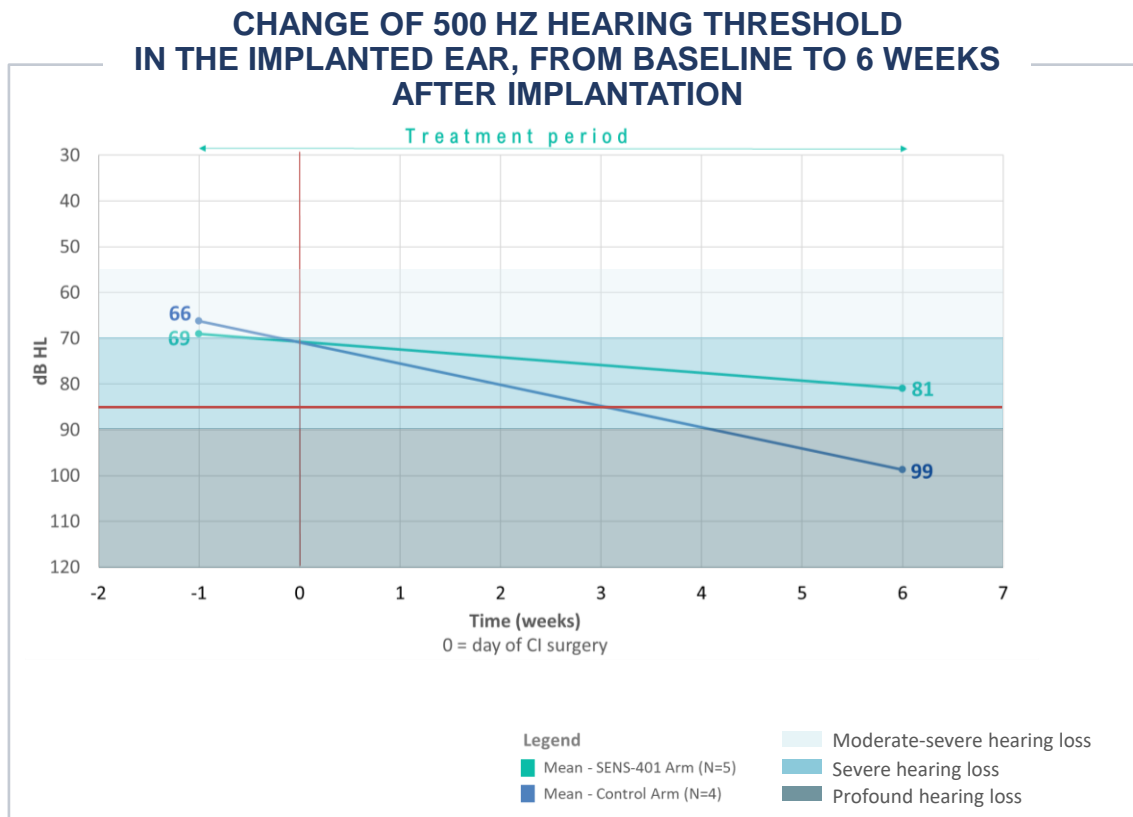
MEAN 3 FREQUENCY PTA CHANGE (250, 500  
AND 750 HZ), IN THE IMPLANTED EAR,  
FROM BASELINE TO 6  
WEEKS AFTER IMPLANTATION



PTA = Pure Tone Average

- A clinically significant difference of 21 dB and 14 dB in the early loss of residual hearing between SENS-401 and control groups is observed at 500 Hz and in the average of 3 frequencies respectively, 6 weeks after cochlear implantation

# SENS-401 Also Preserves Post-Operative Hearing - As Measured at the End of the Treatment Period



— Postoperative hearing preservation defined as unaided air-conduction thresholds <85 dB HL (adaptation of Jensen et al., 2021)

- The SENS- 401 treated group remains above the defined threshold of postoperative hearing preservation
- Shift in hearing loss degree: patients not treated with SENS-401 are progressing from moderate-severe hearing loss to profound hearing loss



# Hearing Preservation Classification System

SKARZYNSKI ET AL. TOWARDS A CONSENSUS ON A HEARING PRESERVATION CLASSIFICATION SYSTEM. *ACTA OTOLARYNGOL SUPPL* 2013

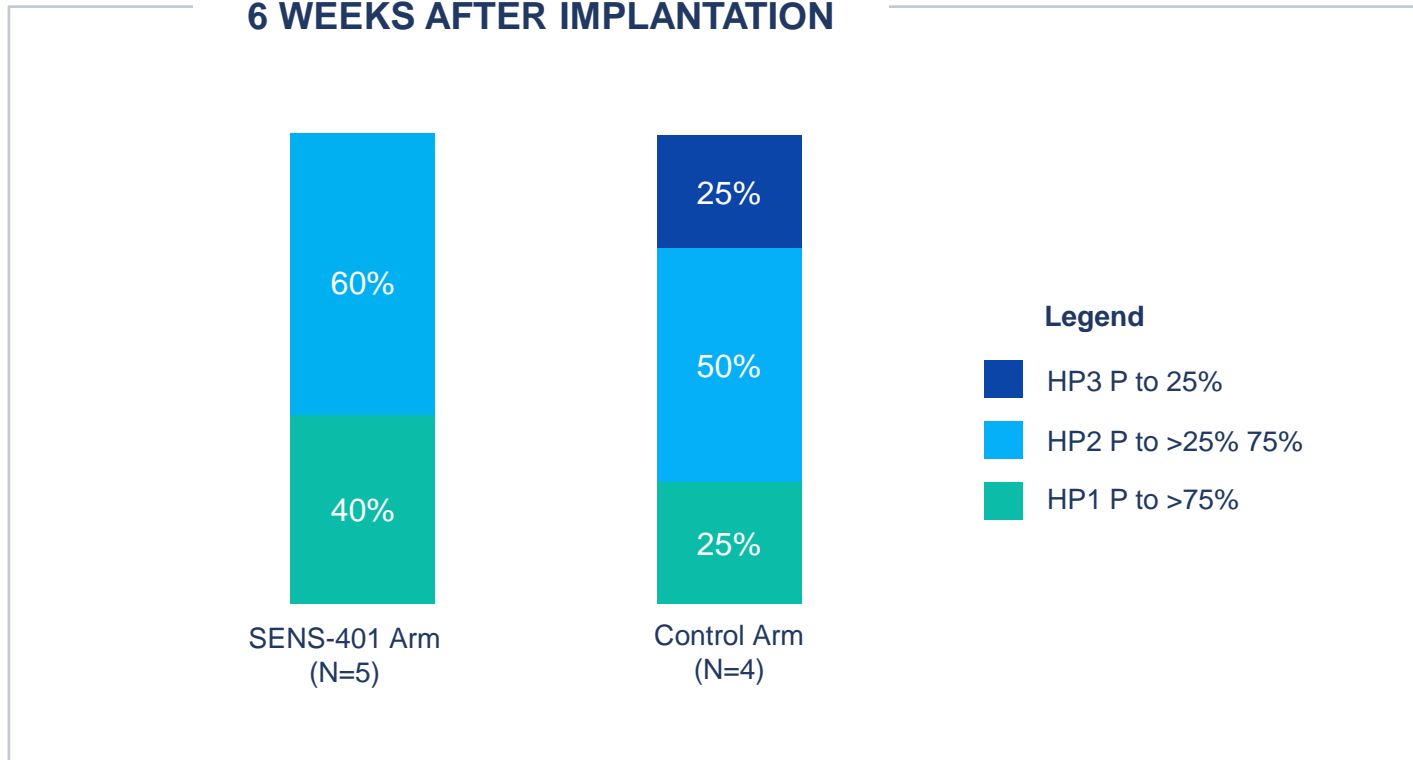
## Criteria

- Classification **independent from users' initial hearing** ► considers pre- and post PTA (Pure Tone Average) thresholds
- Appropriate for all **cochlear implant users** with measurable pre-operative residual hearing
- Covers the **whole range of pure tone average** from 0 to 120 dB HL
- Easy to use and easy to understand

Category	Preservation	HP
HP1	Complete or near-complete preservation	> 75%
HP2	Partial preservation	> 25 to 75%
HP3	Minimal HP	0 to 25%
HP4	Loss of hearing/No hearing	No measurable hearing

# SENS-401 Completely Preserves Hearing in 40% of Patients Treated at the End of the Treatment Period

HEARING PRESERVATION  
6 WEEKS AFTER IMPLANTATION



- Six weeks after surgery, partial (HP2) to complete hearing preservation (HP1) was observed in 100% of patients in the SENS-401 treatment group compared to 75% in the control group, **and no minimal hearing preservation (HP3) in the treated group**

# Conclusion



Preliminary key results are promising and suggest that **SENS-401 can cross the labyrinthine barrier to target cochlear hair cells.**



**Six weeks post-cochlear implantation, the residual hearing loss** whether assessed at 500 Hz or across an average of 3 consecutive frequencies **exhibited a clinically significant, favorable trend for the treated group, in comparison to the untreated group.**



This supports the assumption that **SENS-401, present in the perilymph fluid, reaches concentrations that are pharmacologically active.**



SENS-401 taken 7 weeks confirms it has a **good safety profile.**



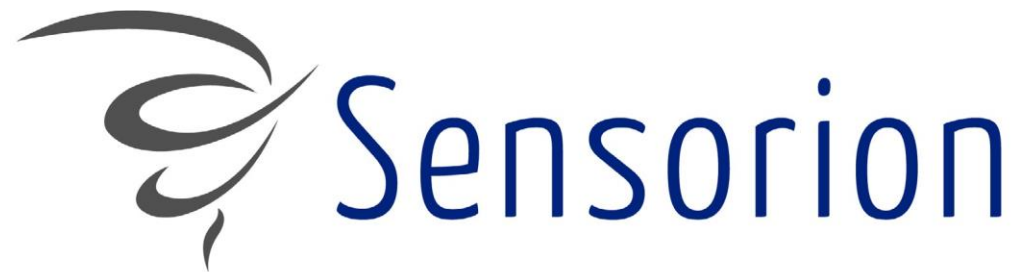
These encouraging trends necessitate further validation across the full study participant group.



**SENS-401 has the potential to modify the outcome of CI while preserving residual hearing by improving speech perception in quiet and noise, music perception, spatial localization and maintaining more natural sound quality.**



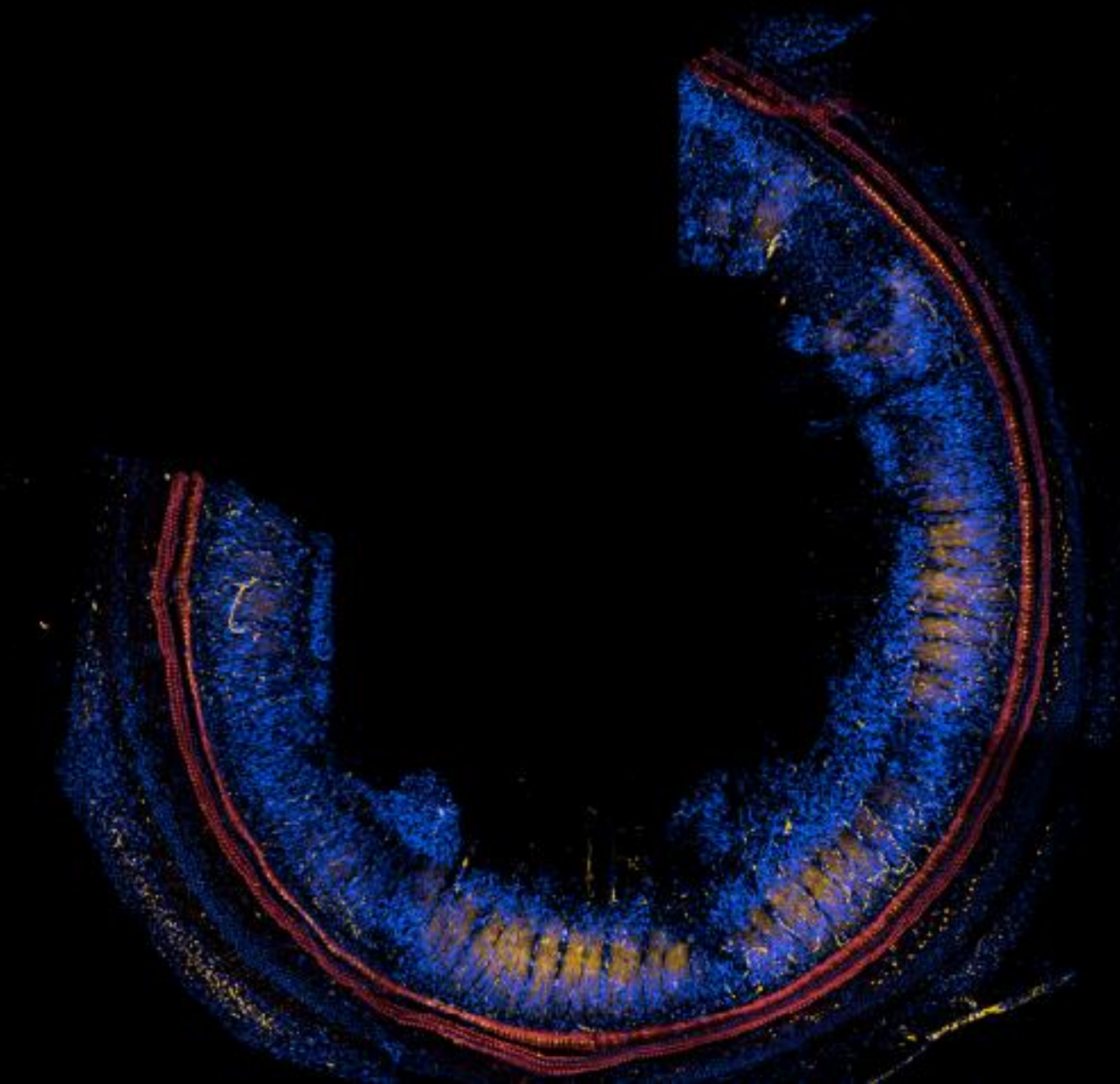
These results support the SSNHL phase 2 data and further development of SENS-401.



## Q&A SESSION CLOSURE

■ Nawal Ouzren  
CEO, Sensorion

July 5, 2023



# Sensorion KOL Webinar SENS-401 to Prevent Residual Hearing Loss after Cochlear Implantation

July 5, 2023

