

Cochlear Implant System

Neuro Zti Cochlear Implant Instructions for Use

For physicians



NEURELEC

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oticon
MEDICAL





“Note”: Indicates a note/tip.



“Caution”: Potential hazard that could result in temporary injury to or hospitalization of the patient/user if not avoided.



“Warning”: Potential hazard that could result in serious injury to or death of the patient/user if not avoided.

Oticon Medical ( NEURELEC) reserves the right to make changes to the design, characteristics and models without prior notice. The only warranty Oticon Medical ( NEURELEC) makes is the express written warranty extended on the sale or rental of its products.

Illustrations are not contractually binding.

This manual provides specific information to the surgical team involved in cochlear implant surgery.



Note: All Instructions for Use are available on the Oticon Medical website.

R_x only Caution: Federal law restricts this device to sale by or on the order of a physician.

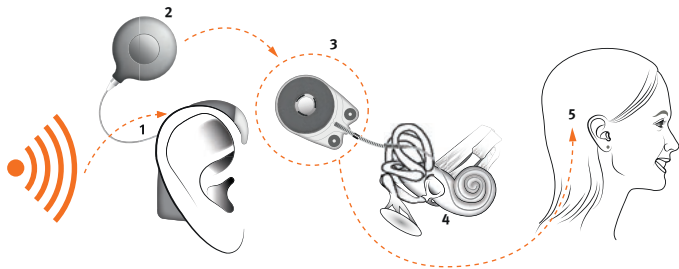
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Description of the Neuro cochlear implant system

The Neuro cochlear implant system consists of an internal (implanted) and external part and can only be used with compatible accessories.



The external sound processor (1) placed behind the ear connected to an antenna (2) that is placed over the implanted part (3) acquires sound from the environment, digitally processes it and sends it wirelessly from the antenna (2) through the skin to the implanted part (3).

The internal implant (3) is surgically implanted under the skin and secured to the temporal bone behind the ear (5). It contains an electronic stimulator that distributes the sound to the electrodes placed in the cochlea (4).

Oticon Medical cochlear implant range

Neuro Zti^{CLA} Version (Ref: M80184) CLA stands for Classic	
Neuro Zti^{EVO} Version (Ref: M80185)	

Identification of the implant

Throughout these Instructions for Use, versions of the Neuro Zti cochlear implant are mentioned only when required.

The Neuro Zti implant can be identified without the need for surgical intervention, only requiring an X-ray (Fig.1). The Neuro Zti implant can be recognized thanks to some visual indicators such as:

- a magnet in the middle of the receiver (one-unit structure)
- a ground electrode is embedded into the lead wire
- the implant is made of only one part as the antenna coil is embedded into the stimulator casing
- two screw inserts



Figure 1: Neuro Zti implant X-ray

Otherwise, the implant can be recognized by using the Genie Medical CI fitting software which will allow retrieving the model and the serial number.

Implant receiver marking:

- Trademark of the manufacturer (Oticon Medical)
- Type of implant (model): the Neuro Zti^{CLA} or Neuro Zti^{EVO} implant version
- Serial number (SN): NZAxxxxx: (NZA) Neuro Zti^{CLA} version + (xxxxx) incremental number
NZBxxxxx: (NZB) Neuro Zti^{EVO} version + (xxxxx) incremental number
- “Bottom”: to specify the skull-facing part of the implant receiver

Magnet marking:

- Trademark of the manufacturer (Oticon Medical)
- Batch number (LOT): YY-XXXXX (YY: Year – XXXXX: incremental number)

Bottom

Side of the receiver in contact with the skull.



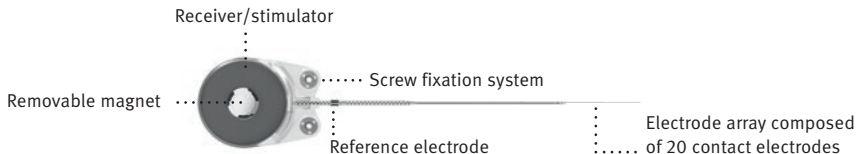
Up

Side of the receiver in contact with tissue.



Main parts of the Neuro Zti implant

The Neuro Zti implant is a single-use device, which comes sterilized by ethylene oxide. Refer to the “Data sheet” section in these Instructions for Use for detailed information on the performance characteristics and safety.



Compatibility

The Neuro Zti implant is compatible with the Neuro 2 sound processor, the accessories specified in this manual, the CI-Link programming system and its related Genie Medical CI fitting software.



Note: Oticon Medical reports on the reliability of its medical devices. Please refer to the reliability report available on the website, www.oticonmedical.com.

Intended use

The Neuro Zti implant is the implantable part of the Neuro Cochlear Implant System.

The Neuro Cochlear Implant System is intended to provide the opportunity to detect and recognize auditory information through electrical stimulation of the auditory nerve, for individuals eighteen (18) years of age or older with bilateral severe-to-profound sensorineural hearing loss who obtain limited benefit from appropriately fitted hearing aid(s).

Indications

The Neuro Zti implant is the implantable part of the Neuro Cochlear Implant System.

The Neuro Cochlear Implant System is indicated for:

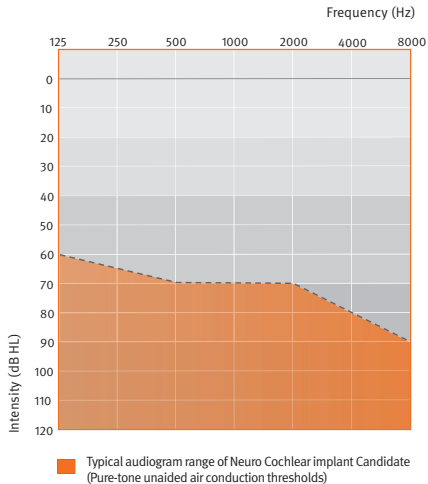
individuals eighteen (18) years of age or older, with bilateral severe-to-profound sensorineural hearing loss, who obtain limited benefit from appropriately fitted hearing aid(s).

Severe-to-profound hearing loss is determined by a pure-tone average (PTA) superior or equal (\geq) to 70 dB HL at 500, 1000 and 2000 Hz. Limited benefit from amplification is defined by scores of 50% or less on Hearing in Noise Test (HINT) sentences in quiet or noise, in the best-aided listening condition.

Unless already appropriately fitted with hearing aids, it is recommended that candidates undergo a hearing aid trial period of three (3) months.



Warning: The Neuro CI system is not indicated for pediatric use, i.e. for children below eighteen (18) years in the United States.



Contraindications

The Neuro Zti implant is the implantable part of the Neuro Cochlear Implant System.

The Neuro Cochlear Implant System is not indicated in the following conditions:

- Absence of cochlear or auditory nerve development
- Hearing loss due to lesions of the acoustic nerve or central auditory pathway
- Anatomic abnormalities, bone growth or fibrosis, preventing the placement of the chosen electrode array inside the cochlea
- Active external or middle ear infections or tympanic membrane perforation in the ear to be implanted
- Presence of medical contraindications to middle-ear or inner-ear surgery or anesthesia as required
- Psychological instability or unrealistic expectations regarding benefits

Undesirable side effects

The candidate should be counseled on possible side effects, including the following:

Risks related to the surgery

- Normal risks associated with surgery and general anesthesia; risks increase in some patients with certain medical conditions.
- Complications associated with surgical procedure, such as skin irritation, infection, meningitis, inflammation, epidural or subdural hematoma, pain, swelling, wound healing complications, CSF leakage, perilymphatic fistula, facial nerve injury leading to transient or permanent facial nerve paralysis.

Risks related to the implant

- Once the implant is in place, the risk of revision surgery or device explantation still exists in case of device failure, decrease of device performance or for medical reasons.
- Loss of residual hearing associated with the electrode array insertion.
- Transient vertigo or dizziness, persistent pain or discomfort, numbness, transient or permanent taste disturbance.
- Stimulation of facial nerve.
- Induction of tinnitus.
- Aggravation of pre-existing tinnitus.
- Unusual pain.
- Perception of uncomfortable sound sensations can lead to a reduction in the number of active electrodes.
- Device may result in uncomfortable, intermittent or non-auditory sensations.
- Electrode array misplacement, magnet displacement.
- Screw migration, electrode array migration, receiver migration.
- Receiver extrusion, electrode array extrusion, magnet extrusion.
- Implant rejection, foreign body or allergic reaction to medical grade silicone, platinum-iridium, or titanium.



Note: *In the case of significant skin irritation, blistering, or signs of skin breakdown, use of the device should be suspended until the wound site can be assessed by the clinical CI caregivers.*

All of these risks have been evaluated, and the materials and design of the implant have been chosen to minimize these risks (improving implant quality to reduce internal failures, screw fixation to prevent device displacement).

Hazards at implantation and during use could be avoided by using the device with precaution and by carefully following all of the recommendations and warnings in these Instructions for Use (e.g. not dropping, immersing, or exposing the device to excessive heat).



Warning: *Do not use the instrument if it is damaged in any way. Do not use if sterile packaging is damaged or already opened. The implant is a non-reusable sterile device and must not be reused.*



Caution: *The healthcare professional should check the integrity of the material before use.*

Patient selection and counseling information

Determining patient candidacy involves a series of tests, evaluations and counseling sessions conducted by health-care professionals. The pre-operative assessment typically includes:

Audiologic evaluation:

A thorough audiologic assessment will be conducted to evaluate whether patients fulfill audiological criteria described in the indications of the device. At minimum, unaided hearing thresholds and best-aided (with appropriately fitted hearing aids) open-set sentence recognition (Hearing In Noise Test - HINT sentences), will be assessed. It is strongly recommended to use hearing aids for a minimum period of three (3) months before considering cochlear implantation. Note that under certain medical conditions, such as infection of the inner ear or ossification, a hearing aid trial may not be needed, and implantation should not be delayed in order to prevent further complications.

Medical evaluations:

Pre-surgical evaluations should assess whether the prospective candidate:

- is in a general health condition allowing surgery, usually performed under general anesthesia.
- does not show any signs of infection or anomalies of the external auditory canal, tympanic membranes or middle ear.
- does not present any cochlear anomalies or other obstacles to electrode placement.
- shows evidence of a functional auditory nerve and no signs of central auditory lesions.

Pre-surgical evaluations will usually involve different medical examinations to evaluate general health condition, an otologic/otoscopic examination and an imaging exam through computed tomography (CT) and/or magnetic resonance imaging (MRI). A CT scan can evaluate middle- and internal-ear anatomy and anticipate access to the cochlea (presence of anatomical abnormalities, obliterations or fibrosis for example). This information will be helpful in determining whether cochlear implantation is indicated and which ear should be implanted. An MRI scan may be needed to further characterize the anatomy of the auditory nerve and central auditory pathways, or identify congenital malformations or early stages of ossification within the scala tympani. In cases of early fibrosis, placement of the electrode array is possible and cochlear implantation is indicated to prevent further development of fibrotic tissues inside the cochlea.



Caution: *Implantation in individuals with complete obliteration of the cochlea due to ossification or similar obstruction is not indicated. Where insertion is possible, the surgeon should note that cochlear ossification, otosclerosis or other fibrotic processes may result in incomplete insertion in some instances. A probe array may be useful in paving a channel for the actual electrode array in cases of fibrosis. In the latter cases, absolute speech perception outcomes may be reduced compared to candidates without otosclerosis, ossification or other obstructions. Clinically, additional programming or rehabilitation may be indicated.*

Meningitis

It is important to consider the risk of meningitis. Meningitis can occur in rare cases but can result in serious illness. Before cochlear implantation, patients should be appropriately counseled regarding this risk. Meningitis vaccine is strongly recommended as it can reduce the risk of developing meningitis. Physicians should provide adequate counseling regarding this risk and review the candidate's vaccination records or verify their immunization status prior to considering implantation.



Warning: *Vaccination recommendations are available on the Center for Disease Control and Prevention website, www.cdc.gov*

Speech and language evaluation:

will assess the patient's overall communication ability including articulation skills, receptive and expressive language abilities, pragmatic/social skills and speech reading skills.

Psychological evaluation:

may be beneficial in some cases when determining cochlear implant candidacy. In particular, psychological evaluation may reveal underlying issues related to the patient's motivation for implantation and expectations towards outcomes.

Intended user profile

The device is intended to be implanted by a physician trained in cochlear implant surgery.

Intended performance

Proper use of the cochlear implant system, including adequate rehabilitation, speech therapy and follow-ups, allows recipients to perceive and make sense of sounds. For individuals eighteen (18) years of age or older, expected benefits include:

- Detection of sounds at medium to loud levels (alerts, environmental sounds, music)
- Understanding speech at medium to loud conversational levels in quiet environments
- Understanding speech in the presence of moderate levels of noise
- In some cases, ability to have conversations over the phone

A clinical study was conducted on performance with the Neuro CI system (refer to the “Clinical trial summary” section for more details). A group of 34 patients was assessed for sound detection and speech recognition before and after implantation with the Neuro CI system at 3, 6 and 12 months after provision of the system.

Participants were tested using only their CI at post-operative appointments, and scores were compared to pre-operative scores obtained in a best-aided condition (with hearing aids for users).

Table 1 on page 13 shows the mean HINT scores, measured in a cochlear implant-only condition at 3, 6, and 12 months post-activation.*

	Pre-op (best aided)	3 months post-op (CI-only ear)	6 months post-op (CI-only ear)	12 months post-op (CI-only ear)
HINT score Quiet	13.3	55.8	64.8	70.1
HINT score Noise at +10dB SNR	13.3	43.8	52.3	57.6
Difference from pre-op (clinical benefit)	–	42.5	51.5	56.8
	–	30.5	39.1	44.3

** Mean scores are reported. Although it is not possible to predict post-implant performance preoperatively for individual patients, clinical data obtained with the Neuro Cochlear Implant System during the clinical study have shown that age at implantation, duration of hearing loss, duration of severe-to-profound hearing loss and preoperative speech perception abilities can have a significant effect on post-implant performance. Please contact your hearing care professional to establish expectations.*



Note: *The Neuro Zti cochlear implant will not restore normal hearing and will not prevent or improve a hearing impairment resulting from organic conditions.*

- In most cases, infrequent use of the device does not allow the user to attain full benefit from it.*
- The use of the device is only part of hearing habilitation and may need to be supplemented by auditory training and instruction in lip-reading.*



Opening the Neuro Zti blister pack

A. Opening the first layer

1



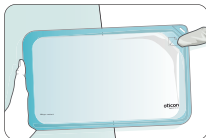
Non-sterile
area

2



Non-sterile
area

3



Non-sterile Sterile area
area

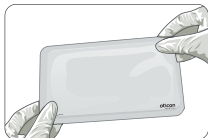
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Non-sterile Sterile area
area

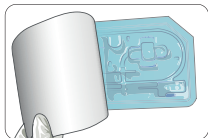
B. Opening the second layer

1



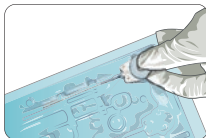
Sterile area

2



Sterile area

3



Sterile area

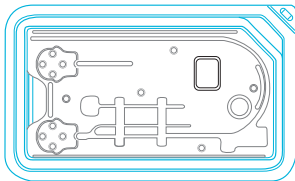
4



Sterile area

Neuro Zti pack contents

- A sterile blister pack that includes: 1 Neuro Zti cochlear implant (Ref: M80184, Neuro Zti^{CLA} version; or Ref: M80185 Neuro Zti^{EVO} version), 1 small box with 3 self-tapping screws (Ref: M80174) (2 screws are used to attach the implant to the bone and 1 spare screw for replacement).



- An envelope that includes: 1 sterile Neuro Zti implant indicator (made of silicone) (Ref: M80180), which is used during the first steps of surgery to verify the correct positioning of the implant under the skin.



- An envelope with printed materials: Instructions for Use, Implantation Registration Form, Explantation Registration Form, Identification Card for patient, labels for patient files.

Surgical instructions

Before implanting the Neuro Zti implant, the physician must become familiar with the technical specifications of the Neuro Zti device and the associated surgical techniques. Before implantation, patients should be informed of the benefits of a cochlear implant, but also of its potential risks (refer to the “Undesirable side effects” section).



Warning: Physicians must carefully read in advance these Neuro Zti cochlear implant Instructions for Use.



Note: Neither the physician nor any person not authorized by Oticon Medical may make changes to the implant design (such as the removal of the fixation system). Unauthorized device modifications void the warranty coverage.

Surgical tools to use for a Neuro Zti cochlear implantation

(refer to the Neuro Zti Surgical Tool Instructions for Use):

Insertion fork (<i>designed for Neuro Zti^{CLA} version</i>)	M80306
Insertion forceps (<i>designed for Neuro Zti^{EVO} version</i>)	M80175
Neuro processor indicator	179994
Neuro Zti implant indicator	M80180
Neuro Zti screwdriver	M80173
Probe array (if needed – to be ordered separately)	M80181
Neuro Zti fixation screws	M80174



Caution: Use only Oticon Medical surgical instruments to perform a cochlear implantation with a Neuro Zti implant.

Surgical steps

A. Determining the optimal Neuro Zti implant version

- The Neuro Zti^{CLA} (stands for CLASSIC) electrode array has a total length of 26 mm (active length 25mm); basal diameter of 1.07mm and tip diameter of 0.5mm. Force measurement studies indicate the Classic exhibits increased stiffness over the EVO array that may aid insertions in cases where the cochlea patency is compromised (ossified cochlea, fibrosis, etc.).
- The Neuro Zti^{EVO} electrode array has a total length of 25 mm (active length 24mm), basal diameter of 0.5mm and tip diameter of 0.4mm, was designed for reduced insertion forces. Reduced insertion forces may facilitate the preservation of cochlear structures.

B. Determining the optimal position of the receiver

Before making the incision for the skin flap, it is recommended to determine the optimal site of the implanted system.

1. Determine the incision line's position

It is recommended to allow sufficient space between the incision and the implant.

The implant's receiver needs to be under the temporal muscle far enough from the auricle of the ear (about 2 cm).

2. Mark the incision line and the receiver's position

To determine the positioning of the implant and of the sound processor, the Neuro Zti implant indicator (M80180–included in the Neuro Zti package) must be used along with the Neuro processor indicator (179994–ordered separately upon request).



C. Measuring the skin thickness and performing the incision



Caution: Skin flap thickness must be up to 8 mm.

If the skin is too thick, a skin flap reduction might be required.



Warning: A monopolar surgical instrument must not be used in case a cochlear implant has already been placed. A bipolar electro-surgical instrument may be used as long as it is not near or in contact with the implant.

D. Determining the final position of the receiver

In some cases, flattening the bone may be required to ensure the receiver remains flat on the bone for a good fixation. First, the Neuro Zti implant indicator (M80180) shall slide inside the periosteal pocket to prepare and ensure an easy progression and the correct positioning of the Neuro Zti implant receiver.



Note: The Neuro Zti implant must be inserted into its final position only after using the silicone indicator as described above.

E. Completing the standard surgical procedure to access the cochlea

When drilling the facial recess to access the cochlea, use of facial nerve monitoring is strongly recommended. Use of neuromonitoring can reduce the risk of damaging the facial nerve.¹

F. Positioning the receiver – Handling the implant

The implant shall be removed from the inner blister pack only after completing the standard surgical procedure up until the round window/cochleostomy.

¹ Neuromonitoring is recommended, particularly where the facial nerve may be at greater risk such as congenital temporal bone anomalies and revision surgeries.

Carefully read the instructions on how to open the implant sterile blister pack (refer to the “Opening the Neuro Zti blister pack” section). We recommend not opening the inner sterile blister pack before it is needed.



Warning: Do not use sharp surgical instruments which could damage the electrode array.



Warning: The sterile state of the Neuro Zti implant must be preserved throughout the different steps of surgery.



Warning: The Neuro Zti implant should be handled with care. The Neuro Zti should be handled by holding the receiver of the implant and not the electrode array. Lifting or holding the Neuro Zti by the electrode array may result in damage to the array.

Orientation of the implant



Warning: The side of the Neuro Zti implant labeled “Bottom” and all markings of the implant shall be placed against the skull and must not be visible.

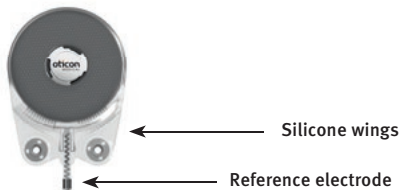


Note: The titanium plate contains important information that identifies the implant (cf. Identification of the implant).

Before attaching the implant receiver to the bone, the reference electrode that is situated on the implant toroid shall be placed in a flat position and remain on the mastoid.



Caution: *The reference electrode must not be placed under the bone; it must stay in contact with tissue.*



Insertion of the receiver

- The receiver must be gently placed into the periosteal pocket (already prepared with the Neuro Zti implant indicator).
- Slide it in by slowly pushing the flexible wings with two fingertips or an atraumatic tool.



Warning: *Do not push in by bending or twisting the silicone wings.*

A. Fixation of the implant

No milling of the bone is needed for the implant bed as the Neuro Zti has a flat skullfacing side and a screw fixation system.



Warning: It is always recommended to secure the Neuro Zti in place with the two self-tapping screws provided in the packaging to prevent any possible displacement or migration, which could create stress and possibly damage the electrode array.



Caution: Follow the steps below to remove the screws from the sterile box and tighten the screws:

- Open the sterile box by sliding the upper cap.
- Insert the screwdriver (M80173 – can be ordered separately) into the screw using firm axial pressure.
- Slowly withdraw the screw from the box.
- The screw is now attached to the screwdriver and can be used.

Position the first screw into one of the fixation system's titanium inserts. It is recommended to hold the screwdriver vertical to the implant axis for fixation. Slowly tighten the screw by using a firm axial pressure with the palm of the hand on the top of the screwdriver. Stop when more resistance is felt. Check that it is secure, then repeat the same procedure for the second screw.

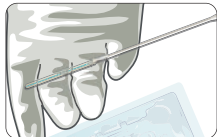
A. Inserting the electrode array



Warning: Carefully remove the protective tubing of the electrode-array before insertion.



Note: To ensure a smooth insertion or in case of a more complex anatomy, a probe array (M80181) can be used before the insertion of the Neuro Zti^{CLA} implant.



Slowly insert the electrode array so that it will follow the cochlear spiral within the scala tympani when inserted. Guide the tip of the electrode array toward the base of the scala tympani using the insertion fork (M80306) for the Neuro Zti^{CLA} or the insertion forceps (M80175) for the Neuro Zti^{EVO}. Then, gradually advance the electrode array using minimal force. Finish insertion by using the silicone extra-cochlear push-rings as a reference. Once insertion is complete, the rings should block the round window/cochleostomy access.



Warning: The electrode array may be secured to prevent the risk of migration. The fixation method and fixation points will depend on the surgical access and the surgeon's preferences.



Warning: The electrode array must be inserted with minimal force. If resistance is felt before reaching the silicone ring, the insertion should be stopped to avoid damaging the structure of the cochlea.

A. Performing the intraoperative objective measurements



Warning: The intraoperative objective measurements must be carried out before or after closure to ensure the implanted device is operating properly.

Intraoperative objective measurements are obtained by using the CI-Link programming system and the Genie Medical CI fitting software. Place the sound processor antenna coil in a sterile sheath, positioned on top of the implant receiver.



Note: Do not touch or press on the external coil while performing the measurements.



Note: *If the skin thickness is less than 4 mm, use the Neuro Zti implant indicator as a spacer on the receiver, above the skin flap.*

A. Performing the closure

B. Performing imaging

It is recommended to perform a scan (Cone Beam CT or X-ray) to check the position of the electrodes in the cochlea.

C. Registering the implant

The Implantation Registration Form must be returned to Oticon Medical within 15 days of the implantation to register and activate the warranty of the implant.

Explantation



Warning: *If a Neuro Zti cochlear implant needs to be explanted due to any condition (medical complication, malfunction, etc.), the system must be examined beforehand by the medical team with help from Oticon Medical clinical support. After joint agreement, please order an explantation kit (Ref: M80183) to correctly return the intact explanted system for further examination, as a special packing needs to be used for these types of shipments (diagnostic specimens shipment). The Neuro Zti implant needs to follow a special waste procedure.*

- If additional clarification is needed for the described procedures, please contact Oticon Medical customer service or local distributor: info@oticonmedical.com.

In order to perform appropriate testing on the device by the manufacturer, it should be carefully removed to preserve it and keep it intact. Special care should be taken for limiting its exposure to cautery procedure, mechanical shock, or electrostatic discharge when explanting and preparing the device for return to the manufacturer.

Ensure the following instructions are performed to properly remove the Neuro Zti implant:



1. First, before removing the device, check its appearance. Any damage or suspected damage should be reported on the explantation form provided with the explantation kit.
2. Second, gently remove the electrode array to limit potential damage to the inner ear. In some cases the electrode array is left in place for future reimplantation or when it is difficult to remove. In these conditions the electrode array can be disconnected from the implant at the lead wire area (between the reference electrode and the push rings).
3. Third, unscrew the two self-tapping screws by using the Neuro Zti screwdriver and turning it counterclockwise to unfix the implant.
4. Carefully remove the Neuro Zti implant and place it in the Explantation Kit.
5. Send back the kit containing the entire device or explanted components (including the implant, array and screws).

If additional clarification is needed for the described procedure, please contact Oticon Medical customer service or your local distributor at info@oticonmedical.com.

The entire device should be returned even if it has been severed or damaged during explant. Please return the electrode array, even if it has been disconnected from the implant. If the array is left in place for future reimplantation, ensure that it is shipped back at that time with a new Explantation Kit.

MRI Safety Information

Magnetic Resonance Imaging (MRI) safety statement

All external components of the Oticon Medical cochlear implant system (BTE, antenna, accessories...) are MR Unsafe and need to be removed prior to MR imaging.	
The implanted components of the Oticon Medical cochlear implant system (Neuro Zti implants) are MR Conditional.	

Prior to undergoing an MRI scan, the patient must contact their treating physician. Any decision to authorize an MRI scan remains a medical decision balancing the risk of damage against the benefit of information provided by the MRI scan.

Any questions or concerns should be clarified with the manufacturer prior to conducting an MRI examination. Full MRI Safety Information is available in these Instructions for Use and in the MRI Checklist, which can be obtained at www.oticonmedical.com or contact Oticon Medical at mri.ci@oticonmedical.com directly.

Non-clinical testing has demonstrated that Neuro Zti cochlear implant is MR Conditional.

A patient with this implant can be safely scanned in an MR system under the following conditions:

MRI Field Strength	1.5 Tesla
Maximum whole-body averaged SAR*	2.0 W/kg
Maximum head averaged SAR*	3.2 W/kg
Maximum Spatial Field Gradient	20T/m
Continuous MR scanning time	15 min

*Specific Absorption Rate (SAR)

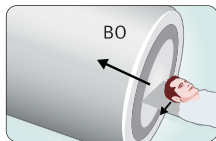
When tested under scan conditions defined above, the Neuro Zti implant produced a maximum temperature rise of less than 2.8 °C during 15 minutes of continuous MR scanning.

- Transmit/receive body coil or a receive head coil can be used.
- A minimum healing period of 2 to 4 weeks after cochlear implant surgery is recommended before undergoing an MRI scan with the Neuro CI system. This delay will allow for wound swelling to reduce to avoid causing any uncomfortable or painful sensation for the patient.
- For all MRI examinations where the patient's head has to be placed in the center of the tunnel, position the patient in a supine position (Figure 1). It is imperative that this position is applied at least 30 cm before the beginning of the tunnel.



Warning: *If the conditions or instructions herein are not followed, injury to the patient and/or damage to the implant may result.*

Figure 1



“Usual position”
with nose up

In non-clinical testing, the magnetically induced displacement force and torque were tested and no safety risk has been identified.



Caution: *Demagnetization of the implant magnet may be possible due to static magnetic fields. To reduce this risk, care should be taken to keep the longitudinal axis of the patient’s head parallel to the scanner’s principal magnetic field. 8% of magnet weakening is expected after several exposures (up to 10). If a significant magnet loss occurs, surgical intervention may be required to replace the implanted magnet.*



Caution: *It is possible that the patient may experience an auditory sensation during an MR scan exam.*



Note: *In non-clinical testing, the artifact size caused by the device extends approximately 50 mm when imaged with a gradient echo sequence and magnet in place. No magnet removal is required, but it can be removed prior to the MRI exam to reduce image artifacts.*

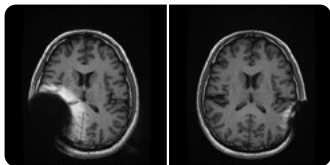


Image: artifacts occurring with (left)
and without the magnet in place (right)

Magnet removal procedure

The magnet may be removed prior to an MRI exam for MRI strengths at 1.5 Tesla to minimize artifacts.

Magnet removal or replacement is a surgical procedure and must take place following standard surgical practice to ensure sterility.

Required tools:

In order to extract the magnet of the Neuro Zti implant, the surgeon will need the three items mentioned below:

- **A Neuro Zti magnet extractor (M80177)** that can be ordered directly from Oticon Medical or the Oticon Medical local distributor. The tool is packed non-sterile. It must be sterilized following the Oticon Medical cleaning and sterilization protocol before performing surgery. Refer to the Surgical Tools Reprocessing Instructions for Use.



- **A Neuro Zti dummy magnet (M80179)**. The dummy magnet is packed sterile. It must be ordered directly from Oticon Medical or the Oticon Medical local distributor before performing a magnet extraction. The dummy magnet is a nonmagnetic casing that is used to avoid any harm caused by strong electromagnetic fields and to reduce artifacts.



Caution: *The dummy magnet should be placed immediately after extracting the implant magnet in order to avoid the ingress of unwanted materials (blood, debris, etc.) into the magnet location on the implant.*





Note: *The cochlear implant recipient should be informed that the processor antenna can no longer be kept in place on the head without the use of an external magnet system or a headband.*

- **A Neuro Zti magnet (M80178)** for replacement. The magnet is packed sterile. It shall be ordered from Oticon Medical or the Oticon Medical local distributor before performing any medical exam that requires a magnet extraction.



Step 1: Make an incision and expose the magnet

Make a small incision to access the magnet. Cut any fibrosis tissue to expose the magnet. The decision about the optimal incision size and location should be made on a case-by-case basis, aiming to minimize the probability of skin-flap complications.



Warning: *In order to avoid potential damage to the electrode array, incisions anterior to the receiver (over the toroid) are not recommended. The incision shall be made on the side of the implant receiver.*

Step 2: Remove the magnet

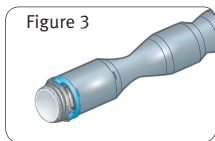
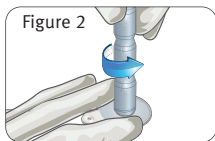
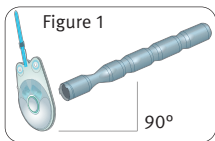
When using the magnet extractor, place it facing the magnet to be extracted.

In order to use the magnet extractor tool, 90° access with respect to the primary plane of the receiver is required (Figure 1).

To grab the magnet that is placed in the implant receiver, insert the three hooks from the magnet extractor tool into the three corresponding grooves in the magnet and lock the magnet extractor tool by slightly turning to the left (counterclockwise) while stabilizing the receiver with your fingers (Figure 2). The magnet will be released from the implant by turning counterclockwise and pulling it.



Warning: Carefully stabilize the receiver with your fingers while removing the magnet.



Note: The magnet extractor tool is magnetic at the point of contact to further assist in extraction (Figure 3).

Step 3: Replace the magnet with the dummy magnet

Remove the dummy from the sterile packaging (Figure 1). Using a finger, push the dummy at the center of the implant receiver until it is in place (Figure 2).



Note: *The dummy magnet is now in place and cannot be removed without the magnet extractor tool.*

Figure 1

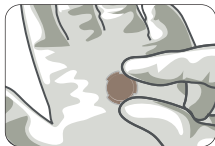
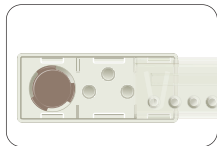
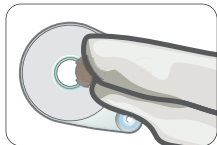


Figure 2



Step 4: Close the incision according to best surgical practice



Note: When using a dummy magnet, the cochlear implant recipient should be informed that the external sound processor can no longer be kept in place on the head without using a headband to maintain the antenna until a new magnet (with magnetic casing) is inserted.

Dummy removal and magnet replacement intervention

Follow the same procedure explained in the “Magnet removal procedure” section.

Magnet replacement

To replace the magnet, follow the same procedure explained in the “Magnet removal procedure” section. Instead of replacing the magnet with a dummy magnet (M80179), place a new magnet (M80178).



Note: Wait until incision is healed before wearing the external sound processor.

This procedure would also be indicated if a patient’s magnet was demagnetized following repeated MRI at 1.5 T.

Patient requisites

- All external components of the implant system (sound processor and accessories) must be removed from the patient’s head.
- If the recipient is a bilateral Neuro Zti recipient, the same procedures outlined in this document must also be followed for the contralateral implant.



Warnings

- If any information is incomplete or ambiguous, or if you have any questions or concerns about the information provided, please contact Oticon Medical customer service or an Oticon Medical distributor.
- This device should only be implanted by surgeons with adequate training in cochlear implantation. Clinical support is made available to assist during surgery.
- The device can only be dispensed to a patient after medical evaluation and with the agreement of a licensed physician (especially for children).
- Implantable device parts shall not be reused if they have been previously implanted in another patient.



Warnings to communicate to the patient

- The patient must be informed of the benefits of a cochlear implant, but also of its possible undesirable side effects (refer to the “Undesirable side effects” section).
- Inform the patient that they must present the identification card prior to any medical examination or treatment.
- Advise the patient to carefully read the instructions for use supplied with his/her sound processor, in particular the section relating to the warnings for use.

- The Neuro Zti implant has a removal magnet. Please advise the patient not to position a magnet on the head in the area of the implant receiver to avoid migration of the magnet.
- Magnets that are not specifically designed for the Neuro system and any other magnetic devices should not be placed on or directly over the implanted components.
- In case of failure or malfunction of the cochlear implant system, the patient should contact his/her implantation center.
- Patients are strongly advised against practicing contact sports (rugby, boxing, American football, etc.) as these activities could result in an impact force that may damage the implanted components.
- Do not dive below a depth of 20 m (~787 in). Excess pressure may damage the implant. In addition, it is strongly recommended not to engage in professional deep-sea diving activities. The implant is not guaranteed against repeated high pressure.



Note: The supplied identification card must be fully completed.



Additional warnings specific to medical interventions/therapies

High-voltage electrical fields:

- **Electrotherapy:** Electrotherapy may send currents of varying strengths. The use of high-voltage electrotherapy techniques is prohibited due to the risk of damage to the implant system. However, low-voltage electrotherapy may be considered as long as the electrodes are not placed in areas near the head or neck.

- **Electroconvulsive therapy:** Do not use electroconvulsive therapy as it can cause tissue damage in the cochlea or permanently damage the implant.
- **Defibrillation:** Sending high voltage through the body is not advised in a patient wearing a cochlear implant.
- **Diathermy:** Medical diathermy using ultrasound, microwave or high-frequency currents cannot be considered in the area of the head and the neck. These treatments can cause cochlear tissue damage or permanent damage to the implant.
- **Neurostimulation:** Do not use neurostimulation directly over the cochlear implant. High currents induced into the electrode array can cause cochlea tissue damage or permanent damage to the implant.
- **Diagnostic tests or treatments using ultrasound:** The implant should not be exposed to the-rapeutic levels of ultrasonic energy. The device may inadvertently concentrate the ultrasonic field and sustain damage.
- **Ionizing radiation:** Ionizing therapy may be used over the implant up to 112 grays; otherwise, it can damage the implant.
- **Electrosurgery:** Do not use monopolar electrosurgical instruments on the head or neck as doing so may induce currents and could cause damage to cochlear tissues or permanent damage to the implant. As soon as a cochlear implant is removed from its packaging in the operating room, any monopolar surgical systems should be turned off to avoid any damage to the implant.
 - Bipolar electrosurgical instruments may be used on the patient’s head and neck; however, they must not be in direct contact with the implant nor be too close.

- **Non-ionizing electromagnetic radiation:**
 - MRI (Magnetic Resonance Imaging). To perform an MRI examination and get full MRI safety information, refer to the “MRI Safety Information” section in these Instructions for Use or to the MRI Checklist which can be obtained at www.oticonmedical.com. Any questions or concerns should be clarified with the manufacturer prior to conducting an MRI examination. Contact Oticon Medical at mri.ci@oticonmedical.com or call +33 (0)4 93 95 18 18.
- **Life-supporting devices**

There is a risk of magnetic interference for patients with life-supporting devices (e.g. cardiac pacemakers, implantable cardioverter defibrillators and magnetic ventricular shunts). In case of abnormal sensation (e.g. altered mental status, headaches, vomiting or loss of consciousness), immediately remove the antenna from your head and contact emergency medical services.

For patients in need of programmable life-supporting devices, it is recommended to place such device at least 15 cm (6 in) from the cochlear implant system.

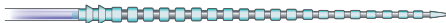
Data sheet – Neuro Zti cochlear implant specifications

Stimulation capacity	
Primary function	Electrical stimulation of the cochlea
Stimulation mode (depending on configuration)	Multi-mode grounding: combined stimulation with monopolar and common ground mode Monopolar for ECAP
Objective measurements	<ul style="list-style-type: none">• Impedance measurement• Electrically evoked compound action potential ECAP

Mechanical properties	
Weight	10.5 g (~0.37 oz)
Dimensions	Diameter: 30.5 mm (~1.2 in) Thickness for Neuro Zti Simulator/Receiver: ranging from 2.95 mm (~0.11 in) to 4.5 mm (~0.17 in) edge to edge
Volume	4.15 cm ³ (~0.24 in ³)
Material in direct contact with human tissue	<ul style="list-style-type: none"> • LSR 40 shore A silicone • HCR 35 shore A & HCR 50 shore A silicone • Adhesive silicone • Platinum iridium 10% • Titanium grade 2 • Titanium grade 5
Receiver	Titanium grade 2 and Zirconia encapsulation
Insulation	Wire: Polytetrafluoroethylene (PTFE) and Polyester (PE) External tubing: Silicone (SI)

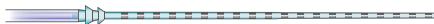
Performance characteristics	
Characteristics of the output signal	Max 5 V
Impedance measurement	Normal values: 500 Ω – 7 k Ω
Skin thickness	Up to 8 mm (~0.31 in)
Essential performance	Accuracy of the electrical stimulation (<10% at C level)
Stimulation frequency	47,500 pulses per second (software limited)
Transportation conditions	Temperature: -30 °C (-22 °F) to +60 °C (+140 °F) Relative humidity: 10% to 90% Atmospheric pressure: 70 kPa (~10.15 Psi) to 106 kPa (~15.37 Psi)
Storage conditions	Temperature: -30 °C (-22 °F) to +60 °C (+140 °F) Relative humidity: 10% to 90% Atmospheric pressure: 70 kPa (~10.15 Psi) to 106 kPa (~15.37 Psi)
Safety	
MRI safety level	Compatible 1.5 Tesla with the magnet in place
Ionizing radiation	Dose max. 112 grays
Methods recommended for determining the functionality of the system	Impedance measurement and integrity test (with collection equipment)
Operating pressure	Absolute pressure of 3 bars (corresponding to a diving depth of 20 meters (~787 in))
Reference electrode	1 cylindrical ground electrode: 17 mm ² (~0.026 in ²) Diameter: 2.1 mm (~0.08 in) Length: 2.5 mm (~0.026 in ²)
Automatic check	Implant identification
Electromagnetic Compatibility (EMC)	ISO 14708-3:2018 Clause 27

Neuro Zti^{CLA} (CLASSIC version)



Specifications and characteristics of the Neuro Zti ^{CLA} electrode-array	
Material components	<ul style="list-style-type: none"> • Connecting wire: Platinum iridium 10% • Stimulation electrodes: Platinum iridium 10%
Number of independent active electrodes	20
Insertion length	26 mm (~1.02 in)
Active length	25 mm (~0.98 in)
Dimensions	Active area: 0.39 mm ² to 0.77 mm ² Diameter at apex: 0.5 mm (~0.02 in) Diameter at base: 1.07 mm (~0.04 in)
Reduced cochleostomy size	Diameter of 1 mm (~0.04 in)
General shape	Straight with shape conforming Straight: distance between electrodes and silicone, inferior to 0.1 mm (~0.04 in)
Shape at the apex	Rounded shape
Shape at the base	Diameter push rings: 2 x 1.5 mm (~0.08 x ~0.06 in)
Insulation	Wire: Polytetrafluoroethylene (PTFE) and Polyester (PE) External tubing: Silicone (SI)

Neuro Zti^{EVO} (EVO version)



Specifications and characteristics of the Neuro Zti ^{EVO} electrode-array	
Material components	<ul style="list-style-type: none">• Connecting wire: Platinum iridium 10%• Stimulation electrodes: Platinum iridium 10%
Number of independent active electrodes	20
Insertion length	25 mm (~0.98 in)
Active length	24 mm (~0.94 in)
Dimensions	Active area: 0.46 mm ² to 0.60 mm ² Diameter at apex: 0.4 mm (~0.16 in) Diameter at base: 0.5 mm (~0.02 in)
Reduced cochleostomy size	Diameter of 0.8 mm (~0.03 in)
General shape	Straight with shape conforming Straight: distance between electrodes and silicone, inferior to 0.1 mm
Shape at the apex	Rounded shape
Shape at the base	Diameter push rings: 1x1.5 mm (~0.04x~0.06 in) & 1 x 1.2 mm (~0.04 x ~0.05 in)
Insulation	Wire: Polytetrafluoroethylene (PTFE) and Polyester (PE) External tubing: Silicone (SI)

Warranty terms and conditions





















Important when implanting

1. The implant is warranted to be free from defects in design or workmanship and is subject to the warranty period defined in paragraph 1.
2. The warranty will be rendered null and void, in part or total, if the device is not implanted in accordance with instructions provided by Neurelec/Oticon Medical, who shall not be held liable, in particular in the following cases:
 - The warranty shall also be void in the event of implant displacement if the implant body has not been attached using the screws (refer to the “Surgical instructions” section in this Instructions for Use).
 - If the implant has not been implanted before the “Use-by date” indicated on the protective packaging (and on the sterile pack).
 - In the event of alteration or voluntary or accidental mishandling, such as impact, exposing the implant to temperatures above +60 °C (+140 °F) or below -30 °C (-22 °F) etc. (refer to the “Package: symbols and meanings” section in these Instructions for Use).
 - If the implant is used even though the sterile packaging has been damaged. The product is sterile and cannot be resterilized. Do not use if sterile packaging is damaged. Do not remove the implant from sterile packaging until required. For shipping, the Neuro Zti outer pack should be packed in a strong and protective cardboard box.
3. Any dispute shall be subject to the exclusive jurisdiction of the courts of Nice, France.
4. The warranty of the device does not cover any misuse of the Neuro Zti cochlear implant before or during surgery. Care must be taken when handling the implant.

Important when explanting

1. Neurelec/Oticon Medical shall not be held liable in the case of explantation due to medical problems (e.g. infection, electrode misplacement, contraindication, etc.).
2. Only explanted patients may receive the new implant under the terms of this warranty.
3. Oticon Medical shall be notified prior to any explantation when a malfunction has been observed.
4. The explanted implant must be returned to Oticon Medical within 15 days in the Explantation Kit obtained through Oticon Medical for an expert assessment, along with the completed medical device report and explantation registration sheet detailing the circumstances of the extraction.
5. Any implant that is explanted shall be technically examined to confirm that the new implant is under warranty.
6. No compensation for damages will be payable regardless of the length of time or loss of use by the explanted patient.
7. The warranty consists of an outright exchange of the defective implant for an equivalent or a more recent generation device.
8. Exchanging an implant under the warranty shall not serve to extend the warranty period of the new implant, nor the replacement of the magnet with a new one.

Package: symbols and meanings

	Fragile; handle with care		Caution
	Sterilized using ethylene oxide		Consult the instructions for use
	Sterilized using steam sterilization		Humidity limitation
	Single-use device; do not reuse		Temperature limitation
	Do not resterilize		Atmospheric pressure limitation
	Serial number		Use-by date
	Catalogue number		Date of manufacture
	Batch code		Manufacturer
	Prescription only		Do not use if the package is damaged
	MR conditional		General symbol for recovery/recyclable Neuro Zti outer pack is made of 80% recycled materials and can be recycled
CE 0459		Marking for European Community with notified body number	

Summary of clinical data

Clinical study

A clinical study was conducted to assess the safety and effectiveness of the Oticon Medical Neuro Cochlear Implant System (NCIS). The clinical study was conducted in individuals eighteen (18) years of age or older with severe-to-profound sensorineural hearing loss. The study was a multi-center, prospective, clinical study that was conducted outside of the US and involved six investigational sites: five cochlear implant centers in Canada and one in Denmark. All patients were followed from the day of their cochlear implant surgery, to one-year after activation of their sound processor, which occurred on average one month after surgery. Patients were treated between February 2, 2017 and December 11, 2018.

Clinical study patient selection

Inclusion criteria

Participants could be enrolled in the study if they met the following criteria:

- Signed written informed consent form prior to any study related activities,
- Aged \geq eighteen (18) years,
- Bilateral severe-to-profound sensorineural hearing loss, pure tone audiometry (PTA) \geq 70 dB HL (average of the thresholds for pure tones at 500, 1000 and 2000 Hz, in both ears),
- Post-lingual onset of deafness,
- Limited benefit from appropriately fitted hearing aid(s), with score \leq 50% correct in HINT sentences recognition in quiet, binaurally in the best listening condition,
- Primary implantation, i.e., not previously implanted (not a previous cochlear implant user who was explanted),
- No anatomical contraindications: Radiological evaluation showing no obstacles to full electrode insertion and verifying the absence of central auditory lesions,
- Fluent in local language, including reading and writing,
- Psychologically suitable,
- Updated pneumococcal vaccine.

Exclusion criteria

Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

- Medical conditions that contraindicate undergoing surgery (middle ear diseases i.e., AOM/CSOM, lesions of auditory nerve, pathologies of central auditory pathway, otosclerosis; any cochlear malformation i.e., Mondini malformation, cochlear ossification, large vestibular aqueduct),
- Unrealistic expectations from the candidate regarding the possible benefits, risks, and limitations that are inherent to the surgical procedure(s) and the device,
- Unwillingness or inability of the candidate to comply with all investigational requirements.

Description of outcome measures

Effectiveness assessment

Clinical effectiveness was evaluated using the Hearing In Noise Test (HINT), which is a standardized sentence comprehension test. The HINT test used in English-speaking cochlear implantation centers in Canada is the same test as the one used in centers based in the United States. HINT sentence scores were measured at 3-, 6- and 12-months after implant activation in two test conditions: 1) Quiet, with sentences presented at an intensity of 60 dB SPL, and 2) Noise, with sentences presented at an intensity of 65 dB SPL, together with a steady speech-shaped noise presented at 55 dB SPL (+10 dB signal-to-noise ratio - SNR).

Clinical benefit was established by comparing scores at follow-up visits obtained in the implant-ear only (i.e., the contralateral ear being obstructed to prevent any hearing), to pre-operative scores obtained in a best-aided configuration (i.e., with well-fitted contralateral hearing aid when applicable). The primary effectiveness endpoint was defined as the clinical benefit in

HINT-Q scores measured at 6 months and a clinical benefit of 20 percent points was considered clinically pertinent (success criterion for endpoint). The other time points with the HINT-Q and all three time points with HINT-N were measured as secondary endpoints.

Safety assessment

In order to assess the safety of the Neuro Cochlear Implant System, all adverse events (major or minor complications) occurring from the surgery to the end of the study were recorded. Major complications (serious adverse events) are those that are life-threatening, those requiring hospitalization and/or resulting in disability or permanent damage, or those requiring revision surgery with or without reimplantation and tinnitus, facial stimulation, pain that could not be alleviated by electrode deactivation; and other serious medical events. Minor complications (adverse events) are those that resolve spontaneously without surgical intervention or with conservative medical management. The primary safety endpoint of the study was defined as the number and proportion of individuals experiencing an adverse event, defined as any major or minor complications. Observed rates of major surgical complications were compared to rates reported in the scientific literature for similar devices.

Clinical Study Results

Patient demographics

Among the fifty-three (53) participants included in the study, 51 were ultimately involved in the safety and effectiveness evaluation. Two patients (of the 53) were excluded from the study for major protocol deviations (one death between inclusion and surgery, unrelated to the clinical study and one surgical failure). The table below reports the main demographic characteristics of the 51 patients involved in the safety evaluation.

Demographics and Baseline Characteristics of all participants

All participants (N)	51 (100%)
Gender	
Female	31 (60.8%)
Male	20 (39.2%)
Age at implantation (years*)	69.5 ± 11.4 [38.0-89.5]
Implanted Ear (side)	
Left	22 (43.1%)
Right	29 (56.9%)
Duration of hearing loss (years*)	
Implanted ear	30.7 ± 19.0 [0.7-71.7]
Contralateral ear	33.2 ± 19.6 [0.7-71.7]
Duration of hearing aid use (years*)	
Implanted ear	22.2 ± 15.8 [0.0-64.6]
Contralateral ear	22.6 ± 15.8 [0.0-64.6]
Average PTA, 500 Hz to 2000 Hz (dB HL*)	
Implanted ear	101.3 ± 13.3 [75-120]
Contralateral ear	95.8 ± 16.3 [70-120]

*Mean ± Standard Deviation (SD) [Min-Max]

Among the 51 patients enrolled, 50 were successfully implanted with one Neuro Zti implant, and were followed one year after surgery for effectiveness and safety assessments. One patient could not be implanted because of a middle-ear pathology discovered during surgery that was not detected before (a cholesteatoma (i.e., keratinized tissue growth in the middle ear or mastoid process)). The surgical procedure for this patient was converted from a cochlear implantation surgery into a cholesteatoma removal surgery.

Among the 50 patients who were successfully implanted, 34 native English-speaking participants were followed for performance assessment, among which 33 completed all speech performance measures. Performance outcomes for one patient could not be assessed due to non-compliance with the follow-up test sessions.

Demographics and Baseline Characteristics in English-Speaking Group

Participants (N)	34
Gender	
Female	19 (55.9%)
Male	15 (44.1%)
Age at implantation (years*)	70.5 ± 12.5 [72.4] [38.0-89.5]
Implanted Ear (side)	
Left	16 (47.1%)
Right	18 (52.9%)
Duration of hearing loss (years*)	
Implanted ear	30.8 ± 18.7 [29.9] [0.7-71.7]
Contralateral ear	31.7 ± 19.7 [33.5] [0.7-71.7]
Duration of hearing aid use (years*)	
Implanted ear	21.4 ± 16.6 [17.7] [0.0-64.6]
Contralateral ear	22.9 ± 16.2 [20.2] [0.0-64.6]
Average PTA, 500 Hz to 2000 Hz (dB HL*)	
Implanted ear	102.6 ± 13.7 [104.2] [75.0-120.0]
Contralateral ear	95.4 ± 15.9 [91.7] [70.0-120.0]

*Mean ± Standard Deviation (SD) [Median] [Min-Max]

Speech perception outcomes and primary effectiveness endpoint

Thirty-four (34) native English-speaking patients had HINT in Quiet scores available pre-operatively. One participant was excluded from follow-up measures for non-compliance with the protocol (discussed above); follow-up measures were therefore performed on 33 patients. In Quiet after implantation, patients understood HINT sentences better with their implant alone than preoperatively in the best-aided condition.

Speech scores in % correct (mean \pm standard deviation)

Test conditions	Test session % correct (mean \pm standard deviation)			
	Pre-operative baseline (N=34)	3-months post activation (N=33)	6-months post activation (N=33)	12-months post activation (N=33)
	Best aided	Cochlear Implant ear only		
HINT Sentences in Quiet (60 dB SPL)	13.3 \pm 16.0	55.8 \pm 31.8	64.8 \pm 27.2	70.1 \pm 24.5
HINT Sentences in Noise (+10 dB SNR)	13.3 \pm 17.7	43.8 \pm 30.6	52.3 \pm 30.0	57.6 \pm 29.9

Three months after activation, average HINT scores rose from 13.3% pre-operatively to 55.8%, progressively reaching 64.8% at 6 months and 70.1% at the 12-months follow-up visit. Scores in +10 dB SNR noise went from 13.3% best aided before surgery to 43.8% at three months, rising to 52.3% at six months, and 57.6% after one year.

The primary effectiveness endpoint of the clinical study was met, a clinical benefit at 6 months, and a clinical benefit of 20% was considered significant (success criterion for endpoint). The clinical benefit at 6 months for HINT-Q was 51.5% (6 months score minus baseline). The one-sided, one-sample t-test gives a significant p-value: $t(32) = 5.5$, $p < .001$, the clinical benefit at 6 months was significantly greater than 20%.

Clinical benefit – stratified analysis

Clinical benefit with the Neuro Cochlear Implant System was defined for the English-speaking participants as the difference between scores obtained at follow-up sessions with their cochlear implant only and pre-operative best-aided scores. In order to obtain details about the distribution of clinical benefit among the clinical study sample, a positive difference between post-implant and preimplant scores exceeding 10 percentage points (pp) was considered as an improvement (“better” category). Similarly, a decrease between pre- and postimplant scores that exceeded 10 pp was considered a worsening (“worse” category). A difference between pre- and post-implant scores of less than 10 pp was considered as no change in performance. Results of this analysis are displayed in the following table. As mentioned before, one patient could not be assessed at follow-up intervals and is referred to as “unknown” in the table.

Sub-group analysis of clinical benefit for the 34 English-speaking participants

HINT Sentences in Quiet (65 dB SPL)	3 months	6 months	12 months
Better (> 10 pp)	76.5% (n=26)	85.3% (n=29)	88.2% (n=30)
Similar (-10 to 10 pp)	5.9% (n=2)	8.8% (n=3)	5.9% (n=2)
Worse (< -10 pp)	14.7% (n=5)	2.9% (n=1)	2.9% (n=1)
Unknown (not measured)*	2.9% (n=1)	2.9% (n=1)	2.9% (n=1)
HINT sentences in Noise (+10 dB SNR)	3 months	6 months	12 months
Better (> 10 pp)	64.7% (n=22)	70.6% (n=24)	79.4% (n=27)
Similar (-10 to 10 pp)	20.6% (n=7)	17.6% (n=6)	17.6% (n=6)
Worse (< -10 pp)	11.8% (n=4)	8.8% (n=3)	0.0% (n=0)
Unknown (not measured)*	2.9% (n=1)	2.9% (n=1)	2.9% (n=1)

*One patient completed HINT at baseline but did not complete it at follow-up visits. The data is missing at random and was not included in the analysis. Omitting this data does not affect the statistical validity of the results.

At the three-month visit, 76.5% of the participants saw improvement in speech perception scores in Quiet compared to their pre-operative baseline, with this proportion rising to 88.2% 12 months after activation. For the speech perception in Noise condition, 64.7% of the participants experienced improvement three months after activation with this proportion rising to 79.4% after 12 months. Only one patient showed a worsening of speech perception scores in Quiet at one year compared to the pre-operative baseline. No patient showed a worsening in Noise at one year.

Other effectiveness measures and analyses

Effect of baseline characteristics on endpoints: Post hoc analysis was conducted to see which, if any, of the six baseline variables (pre-operative PTA, pre-operative HINT scores, age, duration of hearing loss of any degree, duration of severe-to-profound hearing loss, and duration of hearing aid use) affected outcome(s). Multivariate analyses revealed that four baseline characteristics (pre-operative HINT scores, age at implantation, duration of hearing loss, and duration of severe-to-profound hearing loss) were each negatively associated with HINT-Q. The inference from these analyses is that a better pre-operative speech score, earlier age at implantation, and/or a shorter duration of hearing loss is associated with better effectiveness performance.

Analysis by study site: The consistency of the primary endpoint was examined across investigational sites by testing for an effect of site in an ANOVA model, based on 34 English-speaking subjects who completed the 6-month speech recognition tests. The results indicated no evidence of site effects on the primary effectiveness endpoint.

Risks associated with the Neuro Cochlear Implant System and primary safety endpoint

The primary safety endpoint was defined as the number and proportion of individuals experiencing an adverse event, defined as any major or minor complications. Safety data was collected through the duration of the study and reflects the type and duration of any adverse event(s) and classified as major or minor complications. Over the study duration, a total of 71 adverse events were recorded (4 major and 67 minor adverse events). Among the 51 patients in the SAS population, 25 (49.0%) experienced at least one adverse event of any kind, and 26 (51.0%) did not experience any adverse event during the course of the study.

Among the 4 major adverse events, 2 were unrelated, 1 was related to the procedure, and 1 was related to the device. Two related major adverse events in total represents an incidence rate of 2/51 (3.9%) (that is, two patients out of 51 patients experienced a related major adverse event). Of the two related major events, the procedure-related event concerned one patient who experienced an exacerbation of a pre-existing chronic obstructive pulmonary disease (COPD) that required re-admission to the hospital for treatment. The subject recovered after 5 days of treatment. With respect to the major adverse event related to the device, the patient experienced the onset of tinnitus (sensation of ringing in the ear). This adverse event occurred in a patient without documented history of tinnitus before surgery. According to the patient, the sensation was mild just after surgery and rose to a moderate level during the study. Despite this adverse event, this patient continued to use his cochlear implant system throughout the entire clinical study.

A total of 67 minor adverse events were recorded in 24 out of the 51 patients (all minor events patient rate: 47.1%). Among these, 31 events were unrelated, while 36 events were device- or procedure-related. Of these 36 events, 20 were related to the surgical procedure and 16 were related to the device. Procedure and device-related events are described, in turn, below.

The 20 minor procedure-related adverse events comprised post-procedural pain (5) in the wound area, or post-operative dizziness (3), post-operative nausea (2), and temporary tinnitus sensation (2). All other events were observed only once: one case of inflammation at the incision site related to a suture knot, a burning sensation at the implant site, a stitch abscess, excessive swelling over the implant, seroma over the skin flap, one hemotympanum (bleeding inside the tympanic membrane), one case of temporary lack of uptake by taste buds, and one case of strange sensation on the tongue (i.e., ageusia).

Sixteen (16) minor device-related adverse events, 13 concerned the implantable part and the most frequently reported events were a sensation of pain (6), usually occurring over the implant zone, or a sensation of dizziness (4), a sensation of hot spot over the device, a subjective balance reduction and one case of intermittent headache. Three (3) device-related adverse events were related to routine use of the Sound Processor: a sore pinna (1), an irritated earlobe (1), and the perception of reverberant sounds after activation (1). In total, all of these 16 events are well-known minor complications associated with cochlear implantation or sound processor use that have been reported in the scientific literature with similar incidence rates.

Explantations

No explantation was observed as part of this clinical study. All 50 implants (in 50 patients) remained fully functional from the beginning to the end of the study.

Real-world evidence as supporting clinical evidence

Published Literature on Sound Processing Strategies Available with the Neuro Cochlear Implant System

Speech outcomes in the main clinical study reported above were assessed with Crystalis CAP and results presented in Schramm et al. (2020). MPIS, XDP are legacy sound-coding strategies/features of Oticon Medical cochlear implant systems. Peer-reviewed publications concerning these legacy features, safety and performance are referenced and summarized below. Studies included individuals aged 18 years or older, implanted with legacy Oticon Medical devices (Digisonic implant with Saphyr sound processor) and with the Oticon Medical NCIS (Neuro Zti implant with Neuro One or Neuro 2 sound processor).

Summary of data from literature on coding strategies

				Word recognition [Signal level, in dB] Mean±Standard Deviation (SD)		Sentence recognition Mean±Standard Deviation (SD)	
Study	Cochlear Implant System	Signal processing	N Subjects	Quiet	Noise	Quiet	Noise
Lazard et al. 2010	Digisonic/ Saphyr	MPIS (XDP)	55	65 dB HL 68.0 ± 30.0	N.A.	65 dB HL 75.0 ± 20.0	N.A.
Borger et al. 2015	Digisonic/ Saphyr	MPIS (XDP)	10	65 dB HL 78.0 ± 12.3	+10 dB SNR 52.0 ± 19.3	65 dB HL 94.0 ± 7.8	N.A.
Bozorg-Grayeli et al. 2016	Digisonic/ Saphyr	Crystalis (XDP)	20	70 dB SPL 80.0 ± 22.0	+10 dB SNR 59.0 ± 22.3	N.A.	N.A.
Schramm et al. 2020	Neuro Zti/ Neuro 2	Crystalis (XDP)	18	N.A.	N.A.	60 dB HL 72 ± 23.5	+10 dB SNR 54 ± 29.7
Franco-vidal et al. 2020	Neuro Zti/ Neuro One	Crystalis (XDP)	41	65 dB SPL 68 ± 24	+10 dB SNR 58 ± 24	N.A.	N.A.



Note: factors such as test setup, listening material, patient etiology and age groups are not matched between the different studies so any valid comparison between studies remains difficult.

Regarding the compression strategy, both XDP and CAP aimed to maximize the information transfer for a given presentation level (XDP) or dynamically adapt to the environment (CAP). When the signal processing was modified (XDP vs. CAP), no effect was observed on speech performance. This is confirmed in studies by Borger et al. (2015) and by Franco-Vidal et al. (2020), showing 59% and 58% word recognition in noise, respectively. The speech recognition performance in quiet 80% and 68% is also consistent with the reported outcomes among the cochlear implant recipients in the existing literature at the same range of sound intensity (Bozorg-Grayeli et al., 2016).

Regarding the performance from channel selection strategy, MPIS and Crystalis, results from all studies indicate acceptable word and sentence recognition in quiet and in noise, all beyond 50%. As expected, performance decreases when the subjects are placed under a noisy environment. The noise was fixed at 10 dB below the speech (i.e., 10 dB SNR). At this level, subjects were able to recognize either words or sentences in noise with similar scores, between 52% to 59% (Schramm et al., 2020; Franco-Vidal et al. 2020; Borger et al. 2015; Lazard et al. 2010).

These data support that the patient performance is acceptable for MPIS XDP, Crystalis XDP and Crystalis CAP.

None of the studies reported any safety issue relating to the sound processing strategies.

Published Literature on Adult Cochlear Implant Users with Severe-To-Profound Hearing Loss

Safety – Major Complications

A major complication rate following cochlear implant surgeries (with cochlear implants from various manufacturers) was extracted from six (6) articles, totaling 1,316 patients (see Table below).

Reference	N (Adults)	Median or Average Age at Implantation	Retrospective Study Range or Prospective	Major Complication Rate (% Patients)
Farinetti et al., 2014	168	51.9	1993-2013	6.0%
Hansen et al., 2010	180	48.5	1982-2007	1.7%
Jeppesen et al., 2013	269	52.0	1994-2010	8.6%
Kuzovkov et al., 2016	24	NA	Prospective	3.0%
Petersen et al., 2018	463	NA	1995-2016	1.9%
Stamatiou et al., 2011	212	47.5	1986-2010	4.7%
Weighted average	-	49.8	-	4.2%
Current Study	51 (SAS)	69.5	Prospective	3.9%

The weighted average rate of major complications in these articles was 4.2%, varying from 1.7% in Hansen et al. 2010 to 8.6% in Jeppesen et al. 2013. During the Neuro Cochlear Implant System clinical study, 2 major complications were reported, leading to an incidence rate of major complications during the study of 3.9%, which is lower than the weighted average from the literature.

Safety – Minor Complications

Three (3) articles, totaling 617 single adult cochlear implant patients reported minor adverse events using similar reporting standards to be directly compared with the data from the Neuro Cochlear Implant System clinical study (see Table below).

Reference	N (Adults)	Retrospective Study Range	Minor Complication Rate (% Patients)
Farinetti et al. 2014	168	1993-2013	21.4%
Hansen et al., 2010	180	1982-2007	55.6%
Jeppesen et al., 2013	269	1994-2010	59.0%
Weighted average			47.8%
Current study			47.1%

The weighted average rate of patients experiencing minor complications was 47.8% across those references. In the Neuro Cochlear Implant System study, we observed a patient incidence rate of all minor complications during the study of 47.1%, among which 39.2% were procedure- or device-related, both values being below the weighted average from the literature.

Effectiveness

Three studies published in the scientific literature presented similarities in terms of patient indication criteria, device use, test conditions (HINT sentences and pre-op in best aided vs. post-op in the CI ear only) and follow-up time points (measures at 3, 6, and 12 months), to be directly compared with the clinical study described above and published in Schramm et al., 2020. The reviewed articles were Balkany, 2007 (55 patients); Buchman, 2014 (13 patients) and Massa, 2014 (130 patients). They included users of cochlear implant systems from three other manufacturers. A statistical analysis performed on the reported HINT scores in Quiet allowed an estimate of the change from baseline at six months in these studies which was evaluated to be 59.2 percentage points in the quiet condition. With a clinical benefit at six months of 51.5 percentage points in the study described above, the Neuro Cochlear Implant System performs within the range of expected benefits for other available cochlear implant systems in the target patient population.

Weighing the risks and benefits

A cochlear implant system is the only available treatment for patients with severe-to-profound chronic sensorineural hearing loss who obtain limited benefit from standard acoustic amplification through hearing aids. All studies mentioned above demonstrate an improvement of speech perception after cochlear implantation in comparison with pre-operative scores. Given that some

adverse events may occur, patients should be carefully counseled about possible complications and the risk of further adverse events such as device failure during the lifetime of the implant. An appropriate clinical follow-up and commitment to rehabilitation are important to ensure optimal device performance and maximize clinical benefit.

Based on this information, the Neuro Cochlear Implant System shows clinical benefits outweighing the risks related to the surgical procedure or to the medical device itself for individuals 18 years of age or older, with bilateral severe-to-profound hearing loss who obtain limited benefit from hearing aids.

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