ABSTRACT

**Objective:** The presence of a cochlear implant is being considered an absolute contraindication for experiments and/or treatments. We aimed to verify TMS (Transcranial Magnetic Stimulation) compatibility of a new generation of cochlear implants.

**Methods:** in a series of experiments, we test if MED-EL cochlear implants -compatible with stable fields of magnetic resonance imaging scanning- are fully resistant even to rapidly varying magnetic fields as those generated by single pulses and low and high-frequency trains of repetitive TMS (rTMS) applied with a figure of eight coil and different magnetic stimulators.

**Results:** With a TMS intensity equal or below 2.2 Tesla (T) the cochlear implant and all its electronic components remain fully functional, even when the combination of frequency, intensity and number of pulses exceeds the currently available safety guidelines. Induced forces on the implant are negligible. With higher magnetic fields (i.e., 3.2 T), one device was corrupted.

**Conclusions:** Results exclude the risk of electronic damaging, demagnetizing or displacements of the studied cochlear implants when exposed to magnetic fields of up to 2.2 T delivered through a focal coil.

**Significance:** they open the way to use focal rTMS protocols with the aim of promoting neural plasticity in auditory networks, possibly helping the post-implant recovery of speech perception performance.

**Keywords:** Transcranial Magnetic Stimulation; TMS; rTMS; cochlear implant; safety.

**Highlights**
- Cochlear implants are a contraindication to TMS.
- Some new-generation cochlear implants are magneto-compatible.
- They can be used with TMS up to 2.2 Tesla and a focal coil.
INTRODUCTION

Hearing Loss (HL) is the partial or total inability to hear and it can occur in one or both ears. Hearing impairments lead to a decrease in the ability to understand spoken language and to an increase of social, personal, work and family difficulties (Lasak et al. 2014). According to the estimation of the World Health Organization (WHO), there are 360 million people worldwide suffering from some kind of HL (approximately the 5% of the entire world population). This number is rapidly increasing due to longer life expectancy and greater global population (Brown 2015). About 12% of whole Italian population suffer from some kind of HL disorders (Altissimi et al. 2014).

A person with disabling hearing impairment has a permanent difficulty hearing sounds greater than 41 decibels (dB), defined by the Hearing Threshold Level (HTL), as for example a regular speech at close distances (Tate 1994). The HTL is calculated by the person’s hearing performance average in his better ear for the four main frequencies (0.5, 1, 2 and 4 kHz). Moderate (HL from 41 dB) to profound deficit (HL from 80 dB) may not allow patients leading a sufficiently satisfying life relationships, if not through educational and psychological techniques and resources. Implantable medical hearing aids should help these clinical populations (Bond et al. 2009).

A cochlear implant is a surgical neuroprosthetic device implanted in patients with a moderate to profound hearing impairment. The timing of reacquisition of language skills after the implantation is variable across individuals, spanning up to six months and more (Kral and Sharma 2012). Some patients acquire the linguistic abilities for a good phone conversation, while others only improve reading skills (Cohen et al. 1999). The logopedic rehabilitation can be long for cochlear implanted patients. The most relevant factor associated to a successful improvement of language abilities is related to neural plasticity mechanisms (Ponton et al. 1999; McKay 2018).
Transcranial Magnetic Stimulation (TMS) is a noninvasive neurostimulation technique, used to modulate cortical activity in the attempt to promote plasticity in cortical networks, besides investigating various cognitive processes (Wassermann 1998; Gough 2005; Miniussi et al. 2010). Repetitive TMS (rTMS) has the potential to change cortical excitability and cause long-term neuroplasticity effects (Ziemann 2004) and might be a valid, yet unexplored, aid for cochlear implant patients for a faster and optimized acquisition of linguistic abilities.

According to the last available international safety guidelines for the use of TMS in clinical practice and research (Rossi et al. 2009) and its recent update (Rossi et al. 2021), the presence of a cochlear implant is an absolute contraindication to the use of any kind of TMS, from single-pulse to rTMS. Indeed, the magnetic and electric fields induced by TMS can cause malfunction in the implant itself, consequently preventing clinical investigations, research or therapeutic interventions to be carried out in these subset of patients.

More recently, a new generation of cochlear implants has been developed by MED-EL: these are theoretically more resistant to external perturbations, such as those due to exposure to intense magnetic fields. These devices are compatible with the use inside the Magnetic Resonance Imaging (MRI) scanner up to 1.5 Tesla (T) (rarely 3.0 T). However, one major difference discerns between the magnetic field of an MRI, known to be static, compared to that induced by a TMS device, which instead rapidly varies in few hundreds of milliseconds. Hence, whether these cochlear implants are resistant also to such kind of perturbations is still unknown.

Here, we tested the integrity of, as well as forces received by, two MED-EL types of cochlear implants with a titanium housing (Mi1000 Concerto and Mi1200 Synchrony models) after the exposition to single-pulses TMS, low frequency (1 Hz) and high frequency (10 Hz) trains of rTMS. In case of rTMS, parameters of stimulation (i.e., the combination of frequency, intensity, number of pulses and inter-train intervals) largely exceeded all the upper limits suggested for a safe use in humans (Rossi et al. 2009).
Moreover, two different TMS devices were used, both connected with a focal eight-shaped coil, with a maximum output of 2.2 or 3.2 T, respectively. To the best of our knowledge, no previous studies have addressed TMS effects directly on cochlear implant devices; therefore, results may contribute in shading knowledge regarding the feasibility to target specific cohorts of patients with rTMS.
METHODS AND RESULTS

The feasibility of the proposed approach has been evaluated in a two-step modality, taking into account both the electrical/magnetic compatibility of the implants and the elicited effects on the patient.

As a first step, we verified the robustness of the implant in the worst possible working conditions during rTMS. We overstressed this phase reaching conditions that are incompatible with the standard clinical use of TMS. With the aim of presenting the most comprehensive evaluation, two aspects were considered: electrical and mechanical compatibility of the proposed approach with safety requirements.

**Electrical and Magnetic Compliance**

*Experiment 1 - Induced Voltage with single-pulses*

As shown in Figure 1 (left panel), the considered implants (MED-EL Synchrony) embed an antenna consisting in 5 spirals with a diameter of about 22 mm. To analyze the effects of the generated magnetic field, without directly exploit the implant to the high magnetic field, we created a mockup device consisting in 5 copper spirals, wrapped around a 22 mm diameter thermoplastic polymer cylinder in ABS (acrylonitrile butadiene styrene) (see Figure 1, right panel). It is worth noticing that only the most external spiral of the cochlear implant has a diameter of 22 mm, the other ones have smaller area. Thus, we over-dimensioned the active area considering 5 spirals with minimum 22 mm diameter.

Firstly, we mapped the induced voltage in the self-made antenna to verify the portion of the TMS coil with the highest magnetic induction. To reconstruct the induced current, an ABS 3D-printed grid was positioned on the figure-of-8 cooled TMS coil (Ates EB-Neuro, with a maximal output of 3.2 T). The grid consisted in a grating of 1 cm spaced bars (2 mm thickness). The grid positioned on the TMS coil is reported in Figure 2 (left panel). To measure the magnetic induction, we moved horizontally and vertically the antenna probe with 1 cm step in accordance with the grill resolution.

[insert Fig. 1 and 2 around here]
To increase the resolution of the mapped field, we repeated the experiment using both an antenna with 30x30 mm and 40x40 mm base: in such a way we obtained 5 mm resolution. The probe coil was positioned parallel to the TMS coil surface, at 1 cm of distance, as depicted in Figure 2 (right panel).

For each position of the coil in the grid, three single-pulse stimulations with the TMS machine were generated at 100% of the maximal stimulators’ output (MSO) and the related induced voltage was measured with a Tektronix TDS3012 oscilloscope. The average of the 3 measures are reported in Figure 3 (central and right panels, using the 30x30 mm and 40x40 mm grid, respectively). In line with the theoretical hypothesis, visually depicted in the Figure 3 (left panel), the magnetic field generated by the TMS coil has the following characteristics:

i) the highest intensity is in the zone between the two toroids, oriented parallel to the horizontal plane (parallel to the TMS coil surface).

ii) In the center of each toroid the field has lower intensity, but the lines are perpendicularly oriented, with respect to the plane.

Since the induced voltage depends on the trigonometric sine of the angle between the coil and the magnetic field, the induced current is higher in the center of the toroids compared to the surrounding when the implant lays horizontally.

Results of these acquisition revealed that for some positions the magnetic field is strong enough to generate more than 70 Volts (V) in the implant antenna. We registered in the former condition (30x30 mm base) that the induced voltage reached a peak of 74,6 V, with an average in this grid point of 74,4 V. Such quantity exceeds the breakdown limit guaranteed by the company for a safe usage of the device, that is 70V.
This was confirmed by an additional test in which we positioned a Mi1200 Synchrony implant (serial number 750617) on the TMS coil surface and stimulated it with the MSO strength. As a consequence, it was electrically damaged. During failure analysis performed by the producer, it was found that the rectifier diodes within the power supply circuit were damaged. The reason is most likely that the inductive loop antenna received a strong signal that overloaded the rectifier diodes.

**Experiment 2 - Copper shielding**

Even if in real application scenarios of a rTMS treatment course the cochlear implant is always farther and the MSO is usually lower than 100%, we made use of a copper shield to keep the cochlear implant safe.

To continue the experimental campaign, keeping the induced voltage in a wider range of safety (it is a good practice being more than seven times under the limit), we added a copper plate (40x40x5mm) between the antenna and the TMS coil. It is worth noticing that in real usage (with patients) the copper shield will be positioned over the cochlear implant to safeguard it from undesired voltage inductions. Also in this case, we considered and evaluated the worst possible condition i.e. a cochlear implant perfectly centered in the highest magnetic field induction point with 1 cm distance.

We repeated the aforementioned measurements assessing a reduction of 90% of the magnetic field induction. In all the tested position the induced voltage was under 8.3 V, eight times under the safety limit. In Figure 4, we depict data of the acquisitions. Due to the dimensions of the copper layer, a single antenna probe was moved in the grid.

[insert Fig. 4 and 5 around here]

Contextually to the reduction of the induced voltage, we verified that the presence of a copper layer does not affect the induced magnetic shape field in the center of the toroids.
To do this, we added an additional probe as shown in Figure 5 (upper panel). The coil, consisting of 3 spirals wrapped around a 2 cm diameter ABS cylinder, was positioned in the point with the maximum magnetic field, with spirals perpendicular to the surface of the TMS coil. In this position, such a configuration maximizes the induced current into the antenna, simulating a real brain stimulation. Note that the number of spirals were reduced down to 3 for a practical reason. The magnetic field strength in this point is the highest, thus, to prevent damages to the measurement instruments, we reduced the system inducing capability. This did not affect the capacity in measure and analyze the magnetic field effects. Measurements confirmed that the presence of the copper plate did not affect the generated magnetic field in the waveform. A comparison of the recorded waveform is visually depicted in Figure 5 (lower panel).

As a further analysis, we examined the interference of the copper plate in all the possible positions over the TMS coil. This experiment simulated a real clinical scenario, in which the exact position of the copper shielding is a-priori unknown. To this end, we placed a probe antenna (4 spirals 1 cm radius) on the center of the TMS coil perpendicularly oriented and we moved the copper plate (40x40x5 mm) with 1 cm steps horizontally and vertically, covering all the grid. For each grid position we delivered three single-pulse TMS with a biphasic impulse (same stimulator intensity and intensity as above), by recording the induced voltage into the probe (simulating the patient’s brain) positioned in the center of the TMS coil. As visually depicted in the Figure 6, the presence of the copper layer minimally affected the effect of the TMS, indeed we observed variation of +/- 0.3 volt.

[insert Fig. 6 around here]

Experiment 3 - rTMS with real implants

As a final step we assessed the capability of the implant in being used in treatments involving rTMS stimulations. To this end, real cochlear implants were utilized.
Five titanium housed cochlear implant devices by MED-EL were used for the experiments: two were Mi1000 model (Concerto, serial numbers 565312 and 552878) and three were Mi1200 model (Synchrony, serial numbers 723229, 750617 and 740255). All testing was performed in air, thus excluding induction in the electrode pathway.

Two different stimulators were used, both of which connected with a standard figure-of-eight coil equipped with a cooling system: A Magstim Super-Rapid, with a maximal output of 2.2 T, and an Ates EB-Neuro, with a maximal output of 3.2 T. All stimulation sessions were carried out at 100% of the MSO. Regarding the stimulation protocol applied, rTMS was implemented at i) low-frequency 1 Hz stimulation for 30 minutes (1800 pulses) and at ii) high frequency stimulation (10 Hz, trains of 4 seconds, with inter-train intervals of 8 seconds, 1800 pulses overall). Both combinations of frequency/intensity and length of stimulation exceeded the upper limits of published safety tables (Rossi et al. 2009), thus they have to be considered reasonably unsafe for humans.

The devices were positioned on the retro-auricular surface of a phantom plastic head, and the intersection of the two wings of the coil was held in direct contact with the titanium chase of the device. For this experiment, the two Concerto, serial numbers 565312 and 552878 were used. The former received 1 Hz rTMS and the latter received 10 Hz rTMS with the Magstim stimulator.

All the tested implants were sent to the MED-EL for an electronic post checking.

To verify the influence of the TMS induced magnetic fields, the following properties of the implants were investigated:

- Resonance frequency of the inductive link coil. The strong time-varying magnetic field induced by TMS is picked up by the coil of the cochlear implant, and it could potentially damage the inductive receiver and the power supply circuitry within the implant.
- Local oscillator frequency generated in an ASIC (Application Specific Integrated Circuit) within the implant. This is the time base for all cortical implants internal signal processing, as well as the stimulation signal.

- Stimulation amplitude: the TMS induced magnetic field will induce currents in the electrodes paths. This current may influence or damage the circuitry generating the stimulation signal, as the electrodes are connected there.

- Telemetry measurement. The TMS induced magnetic field will generate currents in the electrodes paths. These currents may influence or damage the impedance telemetry circuitry as this circuitry is connected to the electrodes’ channels.

All the implants resulted completely functioning and with no damages/defections, irrespective to the applied protocols of stimulation.

*Experiment 4 - Induced Forces*

Finally, we took into consideration possible induced forces on the device due to the electromagnetic stimulation effects.

It is well known from that the magnetic field pulse generated by the TMS coil exerts attractive forces on ferromagnetic objects and repulsive forces on non-ferromagnetic conductors (Rossi et al., 2009). Therefore, TMS can result in forces on the implant that could potentially displace it. The forces on ferromagnetic objects tend to be larger than those on non-ferromagnetic conductors. Titanium skull plates are non-ferromagnetic and have low-conductivity, and may have radial notches which reduce the induced force. In what follows we report the experiments carried out to assess the compatibility of the aforementioned devices with TMS stimulations.

To this end, we exploited a system based on the ballistic pendulum principle. This is a widespread approach to indirectly measures the impulse (the integral of a force over the time interval for which it
acts). It is worth noticing that measuring the impulse rather than the force better explain the effect of the TMS generated magnetic field on the implant.

A device was positioned at one of the extremities of a PVC (Polyvinyl chloride) pipe (internal radius 16 mm, external radius 18 mm) housed in a 3D printed ABS support, as depicted in Figure 7. The other extremity of the pipe was firmly attached to a 500 CPR encoder (Agilent HEDS-9140). Three different rods with the following characteristics were exploited:

- **rod 1**: length 25 cm, weight 41 grams (rod: 22 g, implant support: 11g, implant 8 g);
- **rod 2**: length 50 cm, weight 62 grams (rod: 43 g, implant support: 11g, implant 8 g);
- **rod 3**: length 120 cm, weight 123 grams (rod: 104 g, implant support: 11g, implant 8 g);

An ad-hoc Labview software was developed to acquire the sensor measurement at 100 kHz. The encoder has two channel quadrature outputs plus a third channel index output, thus we can appreciate variation with a resolution of 0.18°. Firstly, we experimentally validated that the distance between the sensor and the stimulation point guarantees absence of interference and magnetic disturbance in measurement. A series of magnetic pulses were generated to verify the assumption.

During the experiment, the TMS coil was positioned 10 mm from the implant. Such a distance was chosen based on the following considerations: i) the tested distance is the best compromise in respect to the positioning of the coil in a real clinical stimulation of auditory cortices; ii) in case of induced forces on the implant, it allows free swing and/or oscillation, which could not be otherwise observed if the coil was in close contact with the implant; iii) we positioned the cochlear maximizing the induced magnetic field.

To investigate the forces induced by the TMS magnetic fields we carried out two different evaluations. In the former, the cochlear implant was stimulated with a single pulse width 100% of the
MSO, in the latter the coil was instead used to generate a train pulse of 10Hz for 2 seconds (both using Ates EB-Neuro coil, with a maximal output of 3.2 T). Ten trials were carried out for each scenario.

The experimental setup is shown in Figure 7, while a Video is available as Supplementary Material.

In all the conducted experiments we did not record any motion of the pendulum. The unique motion was noticed (and recorded) during a stimulation with the 50 cm rod with an angle of 0.18°. Since the recorded motion corresponds to the resolution of the encoder and it happened once, we considered this as an outlier due to external factors like windage, environmental vibrations, etc. On the base of this results, we can consider the forces induced by the TMS on the cochlear implant negligible.
DISCUSSION

The present study shows the feasibility of TMS and rTMS in proximity/contact to new generation cochlear implants, without producing neither malfunction of the device nor significant forces that could potentially lead to the displacement of the device, which normally is positioned on the temporo-parietal region of the patient’ head and fixed to soft tissues. However, results also suggest that to maintain the implant in an admissible range of electromagnetic safety, an additional tool has to be adopted. We propose here to use a small copper plate to be positioned over the cochlear implant, with the function of shielding it from the electromagnetic field generated by the TMS coil. Repetitive TMS stimulation quickly results in copper plate heating. A simple heat sink is required to avoid replacements of the copper shield or interruptions of the treatment. We exploited a lightweight ABS shell for enclosing the copper layer. Is such way, the temperature of the copper remained far from annoying the patient.

Indeed, the direct stimulation of the device with the Ates EB-Neuro stimulator, capable of reaching a MSO of 3.2 T with the figure of eight coil, damaged the internal circuitry of a previous cochlear implant used for testing purpose. Notably, these data have been obtained with parameters of stimulation (intensity, frequency and timing) exceeding the upper limits of safe use of TMS in humans (Rossi et al. 2009), and can therefore be reasonably extended to every combination used in clinical and research studies.

Even in absence of damage of the internal device circuitries when the induced magnetic field derives from impulses, it is important that forces consequent to the impulse do not impact on the implanted device, which is anchored to the patient’s soft tissue of the skull. Indeed, the magnetic field pulse generated in the coil may exert attractive forces in case of ferromagnetic objects and repulsive forces on non-ferromagnetic conductors (Rossi et al. 2009; 2021). Therefore, rTMS can result in forces on head implants, especially if positioned superficially as cochlear ones, that could potentially displace
them. We measured the momentum (the integral of the force over the time) induced in the cochlear implant with a high-resolution ballistic pendulum. This allowed to measure, even in a such of an unfavorable situation in terms of stability, negligible forces with the TMS pulse (or train of pulses). Thus, it is reasonable to assume that once the device in anchored on the patient’s tissues, such forces are absent or in the very worst case insufficient to displace it.

We did not measure directly the currents induced through the electrodes connected with the implant during the TMS pulses, but we experimentally overestimated them with a mockup device. However, this possibility cannot take place in real-life condition as it is exactly precluded by the safety protection action of the rectifier diodes. Therefore, the event that induced currents in the intracochlear electrodes could theoretically produce damage to cochlear receptors or unpleasant auditory sensations is not possible.

In clinical and research terms, current results open the possibility to use traditional single-pulse TMS in patients with cochlear implants whenever necessary for neurophysiological investigations. Moreover, they open the way for neuromodulatory rTMS applications on auditory cortices in post-implanted patients, possibly aiming at promoting plasticity mechanisms that may aid recovery processes towards earlier and better speech perception performances. Pre-implant rTMS may remain another strategy for improving both short and long term outcomes. Such kinds of clinical trials are under way at Siena University Hospital.

CONCLUSIONS AND LIMITATIONS

New generation cochlear implants that have been highly stressed through rTMS protocols exceeding safety guidelines resulted intact and fully functional, giving the possibility to patients wearing such devices to be enrolled in protocols using magnetic stimulation intervention.
A limitation of the study is that results obtained on the MED-EL devices are not generalizable to all cochlear implants available on the market. Therefore, similar testing to those performed in the present study should be carried out on any other cochlear implant device in order to verify its compatibility with TMS and rTMS, even if already compatible with the exposure to static magnetic fields of the MRI. Similarly, for the delivery of TMS and rTMS we used only a focal eight-shaped coil; therefore, current safety data do not generalize to other coil types.

Acknowledgments

The research has been supported by MED-EL (Elektromedizinische Gerate Gesellschaft m.b.H., Innsbruck, Austria), that also provided the cochlear implants used for testing.

We want to thank Prof. Valerio Biancalana for the precious and helpful indications and suggestions.

Conflict of Interest

All authors report no conflict of interest. We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.
REFERENCES


Figure Legends

Figure 1. Left panel: one of the MED-EL cochlear implants used in the study. Right panel: the mockup exploited for the preliminary experimental evaluation.

Figure 2. The thermoplastic polymer grid in ABS (acrylonitrile butadiene styrene) used for precisely positioning the probe.

Figure 3. Left panel: the theoretical direction of the magnetic field generated by the two toroids inside the coil. The induced voltage mapped with a 30x30 mm and 40x40 mm grid are reported in the central and right panel, respectively.

Figure 4. The voltage induced in the antenna with a copper plate inserted between the antenna and the coil.

Figure 5. The induced voltage in a perpendicular antenna made of 3 spirals. In the upper panel the grid, the sensing antenna and the copper layer are reported. In the lower panel, the waveforms generated by the Transcranial Magnetic Stimulation (TMS) are reported in red and blue using the TMS with and without the copper plate, respectively. It is worth noting that the waveforms have the same profile, thus the same effect. The marked difference in amplitude is due to the presence of the copper layer.

Figure 6. Squares represent the position in which the copper plate was positioned. The color of the square indicates the voltage induced in the coil positioned in the center of the coil. Gray squares represent unavailable measures since the zone was occupied by the probe coil and there was no space for correctly positioned the copper plate.

Figure 7. Setup for the experimental evaluation for evaluating the induced forces. In the left panel the pendulum with 120 cm of rod, in the right panel the 50cm version.

Video 1. Measurement of forces induced on the implant mounted on a pendulum by the induced field of the coil.