Effects of Intraoperative Cochlear Implant Electrode Conditioning on Impedances and Electrically Evoked Compound Action Potentials

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Abstract—*Objective:* **The current study investigates whether, during a Cochlear Implant (CI) surgery, conditioning (i.e. applying short bursts of electrical stimulation) within a saline solution can have positive effects on subsequent intra-operative measurements. We hypothesize that, based on previous research, the impedance values will be reduced, and that the reproducibility of Electrically Evoked Compound Action Potentials (ECAPs) is improved as a result of conditioning.** *Methods:* **We conditioned half of the electrode contacts, within a saline solution, before CI insertion, using 23 MED-EL implants. Impedance was measured for both the conditioned and non-conditioned groups at five time points. Repeated ECAP recordings were measured and compared between the conditioned and non-conditioned groups.** *Results:* **Impedance of the electrode contacts were reduced by 31% after conditioning in saline solution; however, there were no clinically relevant differences after the implantation of the electrode array. The hypothesis that measurement reproducibility would be increased after conditioning could not be confirmed with our data. Within the saline solution, we observed that 44% of the electrode contacts were covered with air bubbles, which most disappeared after implantation. However, these air bubbles limited the effectiveness of the conditioning within the saline solution. Lastly, the effect of conditioning on the reference electrode stimulation was approximately 16% of the total reduction in impedance.** *Conclusion:* **Our data does not suggest that intraoperative conditioning is clinically required for cochlear implantation with MED-EL implants. Additionally, an in-vivo ECAP recording can be considered as a method of conditioning the electrode contacts.** *Significance:* **We confirm that the common clinical practice does not need to be changed.**

Index Terms—**Air bubbles, AutoART, cochlear implant, conditioning, ECAP, electrically evoked compound action potential, electrode array, impedance, surgery.**

I. INTRODUCTION

CLINICAL care with a Cochlear Implant (CI) is a routine treatment for patients with a high degree of sensorineural hearing loss and/or deafness [1], [2], [3]. During the CI surgery, various technical and physiological parameters are typically measured, such as electrode contact impedances, Electrically Evoked Compound Action Potentials (ECAPs) and – less often – stapedius reflex thresholds and electrically evoked auditory brainstem responses [4]. These parameters can then be used for postoperative adjustments made to the CI allowing (1) to improve the postoperative management [5], [6]; and (2) to examine the integrity of the CI. A relationship between electrode impedance and residual hearing is discussed [7], [8]. Electrode conditioning is also available from other manufacturers. However, the procedure used in each case is different. At Advanced Bionics, electrode conditioning is possible and can be carried out in awake patients. The stimulation does not lead to an unwanted loud perception, so we suspect the stimulation current is not too high. With Cochlear, on the other hand, the electrode conditioning is carried out in an intra-operative mode in the corresponding software (Custom Sound EP). The electrode conditioning can be performed in the Auto-NRT/Advanced-NRT task to ensure better measurement conditions by the expected reduction of electrode impedance. The user can freely adjust the stimulation current level. It is important to note that electrode conditioning, in Custom Sound EP, should only be performed in sedated patients due to the fact that the stimulation can lead to unpleasant perception of volume.

Intracochlear electrode array contact surfaces are made of platinum, a material that is known to be bio-compatible and suitable for chronic electric stimulation [2]. When such electrode contacts are initially used within the human body, their properties (e.g. impedance) change until a quasi-stable electrical condition is reached. The terminology used for intentional electrical stimulation, to achieve the desired quasi-stable electrical condition has not been consistently used throughout the literature, and it has often been referred to as "surface activation", "conditioning", "stabilization", "initial stimulation",

"electrochemical cleaning", "depassivation" and/or "burn-in". However, throughout the course of this manuscript we will use the term conditioning, which commonly lasts in the order of some seconds (depending on the stimulation pattern used [9]). Previously, during a CI surgery, performing both electrode impedance and ECAP measurements was recommended [10]. Both of these telemetric measurements [11] make use of intra-cochlear electrode contacts of the CI. Thus, we wanted to address the question as to whether conditioning of an electrode array would be beneficial for those recordings performed during a CI surgery. Beneficial in this case means that impedances are lower and recordings more reproducible. Currently, several clinical approaches exist in terms of treating CI electrodes during surgery: (1) no conditioning; (2) conditioning just before implantation in a petri dish or implant package filled with saline or ringer solution (in-vitro); or (3) conditioning after implantation in the participant (in-vivo) [12].

The electrode impedance is primarily related to resistive characteristics of the surrounding tissue, with low impedance indicating good contact between the electrode surface and the tissue [13]. Whereas high impedance could induce artifacts within the audio-physiological measurements [9], [14]. It was shown by Müller-Deile that the conditioning of CI electrodes, manufactured by Cochlear Ltd. (Sydney, Australia), can considerably reduce the impedance of the contacts [9]. For CIs manufactured by MED-EL GmbH (Innsbruck, Austria) [15], conditioning is performed during the production process by applying high rate, high amplitude stimulation on all channels for several minutes while the implant is immerged in saline solution. However, it is known that the effects of the electrode conditioning are partly reversible, primarily occurring when the electrode contacts are unused for extended periods of time [9]. Coincidentally, throughout the storage and shipping of CIs, these electrode contacts remain unused, thus potentially reversing some beneficial effects of conditioning.

Therefore, in this study we sought to analyze the effects of additional conditioning treatment directly prior to cochlear implantation. We aimed: to use in-vitro conditioning using a saline solution within a sub-set of electrode contacts; to measure the effect of conditioning on electrode impedance and test-retest accuracy of ECAP recordings; and to execute an intra-implant comparison of conditioned vs. non-conditioned electrode contacts. We hypothesized that, based on previous research: (1) the impedance values are reduced after conditioning; and that (2) the test-retest reproducibility of ECAPs is improved by conditioning.

II. METHODS

A. Ethics

This study was approved by the ethics committee of the Universitätsklinikum Schleswig-Holstein, Campus Kiel (No. D488/19) and the ethics committee of Universitätsmedizin Rostock (No. A 2019-0105). All participants provided verbal and written informed consent prior to testing. All protocols were performed in adherence with the standard set in the latest revision

TABLE I
PARTICIPANTS DEMOGRAPHICS

Age	Gender	Side	Electrode
78	male	right	FLEXsoft
57	male	left	FLEXsoft
44	male	left	FLEXsoft
61	female	right	FLEXsoft
40	male	left	FLEXsoft
53	female	right	FLEXsoft
71	female	left	FLEX28
61	female	left	FLEXsoft
51	female	right	FLEXsoft
50	female	right	FLEXsoft
75	female	left	FLEXsoft
72	male	left	FLEXsoft
75	male	right	Standard
51	female	left	FLEXsoft
66	male	right	FLEXsoft
30	male	left	FLEXsoft
57	male	right	FLEX28
30	male	left	FLEX28
44	male	right	FLEXsoft
75	male	left	FLEXsoft
67	female	right	FLEXsoft
80	male	right	FLEX28
50	female	right	FLEX26

of the Declaration of Helsinki (except for the registration in a database).

B. Participants

23 (10 female, 13 male, age 30–80 years, mean of 58.2 years) post-lingual deafened adults, who at the time were undergoing a CI surgery in two different CI centers (Universitätsklinikum Schleswig-Holstein, Campus Kiel and Universitätsmedizin Rostock), volunteered to take part in this prospective, cross-sectional study. Participants were included if they had selected a MED-EL manufactured CI, if they were ≥18 years, not pregnant, and had not participated in any pharmacological clinical trial within four weeks prior to enrolment. All implants were MED-EL Mi12xx devices and had 12 electrode contacts with contact 1 being the most apical contact and contact 12 the most basal. For the FLEXsoft, FLEX26, and Flex28 electrode arrays, contacts 1 to 5 are single contacts, whereas contacts 6 to 12 are double contacts but have the same overall surface area [16]. For the Standard electrode arrays, all contacts are double contacts. Participant characteristic data are outlined in Table I.

C. Equipment and Electrophysiologic Measures

The recordings were performed using both clinical hardware (MED-EL MAX programming interface) and software (MAESTRO version 8.0.x by MED-EL in "Intraoperative session" mode). A sterile saline solution (NaCl) was poured into the implant package after opening to perform the in-vitro impedance measurement as well as conditioning directly before implantation of the electrode array.

Impedance recordings: Impedance was recorded using the Impedance Field Telemetry (IFT) task of MAESTRO. IFT measures the voltages Fig. 1 during biphasic, cathodic leading stimulation pulses (amplitude of 302 current units corresponding
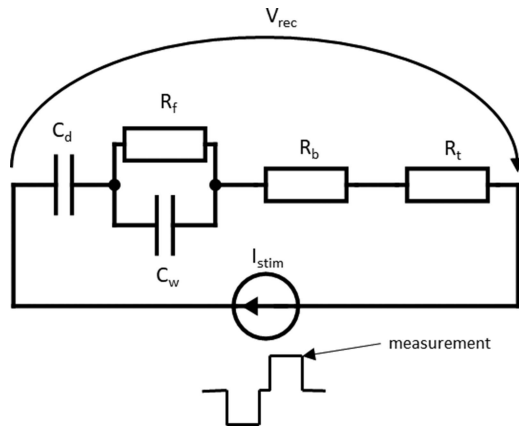
Fig. 1. Electrically equivalent model for the interface impedance of a contact. C_d is the decoupling capacitor. C_w (Warburg capacitance) and R_f (Faradic resistance) and R_b (bulk resistance) are modelling the electrode-electrolyte interface for one intracochlear contact. R_t is the tissue resistance between the stimulating electrode and the reference electrode on the implant housing [17], [20].
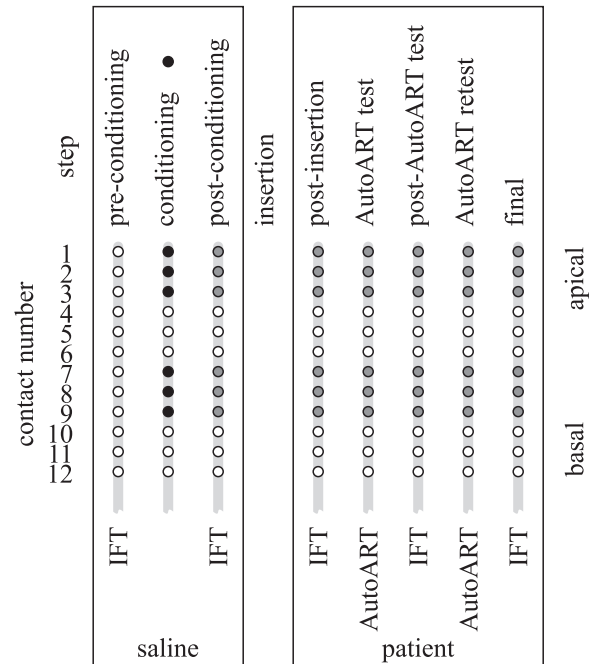

Fig. 2. Clinical and measurement procedure is schematically presented. Steps were conducted from left to right. Filled black dots indicate electrode contacts that were "conditioned".

to 302 μA with a phase duration of 24 μs) throughout all combinations of stimulus and recording contacts to determine impedance of the electrode contacts. The recording (V_{rec}) takes place at the end of the second (anodic) phase Fig. 1 [17], [18], [19].

Electrically Evoked Compound Action Potential recordings: ECAPs were measured using the Automated Auditory nerve Response Telemetry (AutoART) task of MAESTRO. We used the default setting which uses monotonically increasing stimulation amplitude (8 nC/s) with biphasic, alternating stimulation pulses from 0 nC to 35 nC at 80 pps [21]. All 12 electrode contacts were then sequentially stimulated in the following order: 6, 2, 11, 4, 9, 7, 1, 12, 3, 10, 5, 8. For a given stimulus electrode contact i, the ECAP recordings are performed on contacts $i-2$, $i-1$, $i+1$, and $i+2$ (if present). The option "Initial pre-check of ECAP presence at maximum charge" was not used during the current investigation.

Analyses of stimulation and recording were performed separately for conditioned vs. non-conditioned electrode contacts:
- Conditioned: Stimulation electrode contacts 1–3 and 7–9.
- Non-conditioned: Stimulation electrode contacts 4–6 and 10–12.

In order to avoid bias, due to the differing number of measurements per participant when ECAP thresholds were not detected for every case, the averaging of ECAP thresholds for the test & retest were performed per participant (i.e. a missing value was accepted). Subsequently, the ECAP thresholds for both recording electrodes were averaged (one missing value was accepted).

D. Measurement and Conditioning Steps

The study was performed during CI surgery and consisted of sequential steps: three steps before and five steps after implantation, see Fig. 2.

Phase duration	27.1 μs
Active channels	1, 2, 3, as well as 7, 8, 9
Stimulation cycles	600 with a rate of 20 Hz (results in stimulation frequency of 15.85 kHz per electrode contact per cycle and a burst duration of 37.9 ms)
Polarity	biphasic pulses with negative initial phase ("cathodic-first")
Timing	sequential
Pulses distance	7 μs
Amplitude	1200 μA (charge 32.4 nC)

Pre-Conditioning: After opening the sterile packaging containing the CI, it was filled with a sterile saline solution until both the implant and all contacts were covered. The receiver coil was attached to the bottom of the package allowing for IFT measurements. After the initial IFT measurement, it was assumed that all contacts with high impedance had an air bubble on their surface. The study protocol allowed for slight movement of the electrode array due to the presence of air bubbles, with the hope that the air bubbles would disappear. The IFT measurements were repeated until no change in the impedance status was noticeable.

Conditioning: Conditioning was completed using the MAESTRO Electrically Evoked Auditory Brainstem Response (EABR) task. EABR allows for the electrical stimulation, using a pre-defined number of bursts on selected electrodes. It must be noted that no brainstem responses were measured within the saline solution. The settings that were used are outlined in Table II.

Throughout the conditioning process, each of the 6 pre-selected electrode contacts were receiving 100 biphasic stimulation pulses at an amplitude of 1200 μA per each burst. Overall, 60,000 pulses per electrode were applied. Contacts 4, 5, 6, and 10, 11, 12 were left non-conditioned. We chose this pattern to have all possible combinations of conditioned and non-conditioned stimulation and recording electrodes available for the upcoming AutoART recordings.

Post-Conditioning: After the initial conditioning, an IFT recording was performed in the sterile saline solution, allowing for the comparison between *pre-conditioning* and *post-conditioning* in order to evaluate the overall effect of initial conditioning.

Insertion: After the *post-conditioning*, the surgeon then inserted the electrode array into the cochlea. There were no additional modifications to the overall surgical technique compared to the standard CI surgery.

Post-Insertion: After insertion, an IFT recording was performed in-vivo to assess the remaining effect of the in-vitro conditioning. Similarly, to *pre-conditioning*, due to the case of air bubbles, this measurement was allowed to be repeated. The final IFT measurement was used for analyses.

AutoART Test: After *post-insertion*, we used the AutoART task, via MAESTRO, to measure ECAPs within all 12 electrode contacts.

Post-AutoART Test: After which, an IFT recording was then repeated to control for the fact that the AutoART task is a form of in-vivo conditioning.

AutoART Retest: The AutoART task was then repeated to compare the reproducibility of the measurement between the conditioned and non-conditioned electrode contacts.

Final: Lastly, an IFT recording was used to test whether the impedances of the non-conditioned group had any further impedance reduction.

E. Analysis

Contacts with air bubbles: All electrode contacts that showed a HI (high impedance) during surgery but a normal impedance during postoperative measurements were assumed to have had air bubbles on their surface. These contacts, during both *pre-conditioning* and *post-conditioning*, could not reliably be considered as conditioned. Therefore, analyses on these contacts were performed as follows:

- For the analysis regarding impedance, all contacts that had air bubbles, at least at one step, were excluded.
- For all ECAP analyses, conditioned electrode contacts were only included if they had no air bubbles during *post-conditioning* (impedance was < 20 kΩ). All non-conditioned electrodes were included. All contacts with air bubbles were excluded in both the *AutoART test* and *AutoART retest* steps.
- All electrode contracts were included when analyzing for the effect of air bubbles.

Statistics: All data were analyzed using the software Python 3.8 (https://www.python.org) with one exception as mentioned below. The factors *group* (conditioned vs. non-conditioned), *step* (as listed in Fig. 2), *participant* (given implant and cochlea) and *electrode contact number* (contact properties and location in the cochlea) are generally considered important for the impedance and the ECAP threshold. We used statistical tests and factors as follows:

- To compare the impedances between the conditioned vs. non-conditioned groups within the same step, two-sided unpaired t-tests were used.
- For conclusions on impedance changes between steps within either conditioned or non-conditioned groups, two-sided paired t-tests were used.
- To learn whether the factor electrode contact number plays a role for the impedance at a given step, a within group Analysis of Variance (ANOVA) was performed (conditioned/non-conditioned). During *pre-conditioning*, due to the same baseline, we combined both groups (conditioned + non-conditioned) to increase statistical power for the ANOVA. For this analysis we used *R* instead of Python with the R package *nlme* to perform a linear mixed effect model (function lme) with the model "impedance $\sim$ channel". Participant was used as random effect.
- We were using an F-test to compare the distributions of test vs. re-test differences of ECAP thresholds between the conditioned vs. non-conditioned groups.

As not all statistically significant differences are clinically important, we defined the clinically relevant changes as follows, based on clinical experience:

Impedances: We considered impedance changes lower than 100 Ω as not being clinically relevant.

ECAP: ECAP threshold changes below 0.5 nC were not considered clinically relevant.

We know that with our methodology, the same data were used in multiple statistical comparisons. This requires a modification of the significance levels like the Bonferroni correction. However, given that the concept of fixed significance levels as such was criticized by many statisticians [22], [23], we keep the commonly accepted level of $p = 5\%$ and follow the recommendation to interpret the result carefully, especially if p is close to that arbitrarily chosen value.

III. RESULTS

A. Measuring Impedances

Fig. 3 shows the impedances in different steps. During *pre-conditioning*, as expected, we saw a similar impedance between both groups (conditioned vs. non-conditioned; p = 0.142) (Table III).

Due to the similar baseline, we combined both groups resulting in a mean impedance of 4.6 kΩ with a standard deviation of 2.2 kΩ. Further analyses (ANOVA) showed no impedance differences between electrode contacts.

During *post-conditioning*, the impedances of the conditioned group were significantly lower compared to the non-conditioned group (3.0 ± 1.4 kΩ vs. 4.7 ± 2.1 kΩ; unpaired 2-sided t-test: t = 5.655; p = < 0.0001; Table III).
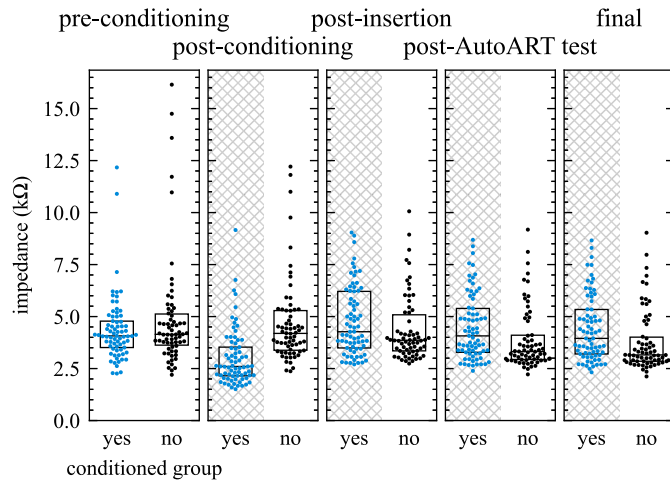
Fig. 3. Boxplot of impedances in different steps. Only values are shown that had no air bubbles in all steps. The shaded areas indicate electrode contacts that were conditioned.

TABLE III
COMPARISON BETWEEN CONDITIONED VS. NON-CONDITIONED GROUPS IN DIFFERENT STEPS

Step	Δ Means	Δ Medians	t-Statistic	p
Pre-conditioning	-553	-75	1.478	0.142
Post-conditioning	-1669	-1590	5.655	8.72e-08
Inserted	407	410	-1.480	0.141
Post-AutoART Test	585	755	-2.232	0.0272
Final	617	795	-2.370	0.0192

After implantation, during the *post-insertion* step, the conditioned group had a nominally higher impedance compared to the non-conditioned group ($4.8 \pm 1.6\,\mathrm{k\Omega}$ vs. $4.4 \pm 1.6\,\mathrm{k\Omega}$). This difference was contrary to what was expected and was above the value of what we considered as clinically relevant.

To answer the question whether the impedance, once implanted (*post-insertion*), depends on the electrode position, we used an ANOVA to compare between the conditioned vs. non-conditioned groups. We found that in both groups the electrode contacts position did have a significant effect on the impedance. Meaning that the effect of the electrode contacts and the conditioning on impedance could not be easily distinguished between during the *post-insertion* step.

B. Direct Effect of Conditioning on Impedance

Before conditioning, the mean impedances of the electrode contacts in the conditioned and non-conditioned group were $4.4 \pm 1.6\,\mathrm{k\Omega}$ and $4.9 \pm 2.7\,\mathrm{k\Omega}$ (*pre-conditioning*, in saline solution, without air bubbles). After conditioning (*post-conditioning*, still in saline solution), the impedance of the conditioned group reduced by $1.3\,\mathrm{k\Omega}$ (standard deviation $1.1\,\mathrm{k\Omega}$), whereas the reduction in impedance within the non-conditioned group was only $0.2\,\mathrm{k\Omega}$ (standard deviation $1.6\,\mathrm{k\Omega}$) (refer to Table IV, Figs. 3 and 4). It must be noted that both groups shared a common reference electrode contact at the CI body which is inevitably conditioned.

TABLE IV
T-TEST RESULTS FOR PAIRED IMPEDANCE CHANGES

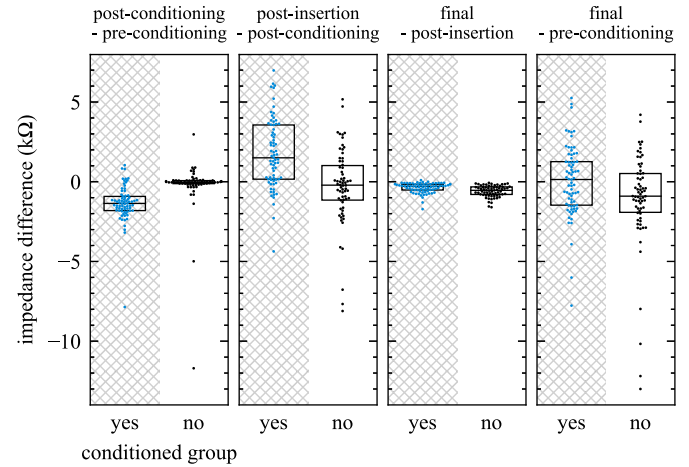| Step A	Step B	Cond.	t-Statistic	p
Pre-conditioning	Post-conditioning	no	1.16	0.251
Pre-conditioning	Post-conditioning	yes	10.4	2.26e-16
Post-conditioning	Inserted	no	1.15	0.252
Post-conditioning	Inserted	yes	−5.82	1.05e-07
Inserted	Final	no	15.1	2.12e-30
Inserted	Final	yes	10.2	2.15e-18
Pre-conditioning	Final	no	3.01	0.00374
Pre-conditioning	Final	yes	-0.0615	0.951

Fig. 4. Paired impedance changes. Only values are shown for electrode contacts that had no air bubbles in all steps.

C. Reproducibility of IFT

To assess the reproducibility of the IFT, we plotted the differences between the steps (Fig. 4). Of special interest was the distribution width of the impedance differences between the first and the last in-vivo steps when comparing the conditioned and non-conditioned groups. We found that the reduction in impedance was similar in both the conditioned and non-conditioned groups (conditioned: $-0.5\,\mathrm{k\Omega}$ and non-conditioned: $-0.6\,\mathrm{k\Omega}$, respectively), and further the standard deviation of the change was similar (conditioned: $0.5\,\mathrm{k\Omega}$ and non-conditioned: $0.5\,\mathrm{k\Omega}$, respectively).

D. Air Bubbles

After the implants were placed in the saline solution (*pre-conditioning*), 122 out of 276 electrode contacts were covered by air bubbles (shown as a high impedance after the IFT task). These included 57 contacts in the conditioned group (not yet conditioned) and 65 contacts in the non-conditioned groups. However, due to the air bubbles, these electrode contacts could not be considered reliably conditioned and were excluded during impedance comparisons, as described above.

After conditioning (*post-conditioning*), the number of air bubbles reduced to 53 in the conditioned vs. 59 in the non-conditioned groups. Moreover, directly after implantation (step *post-insertion*), the number of air bubbles dropped to 2 in the
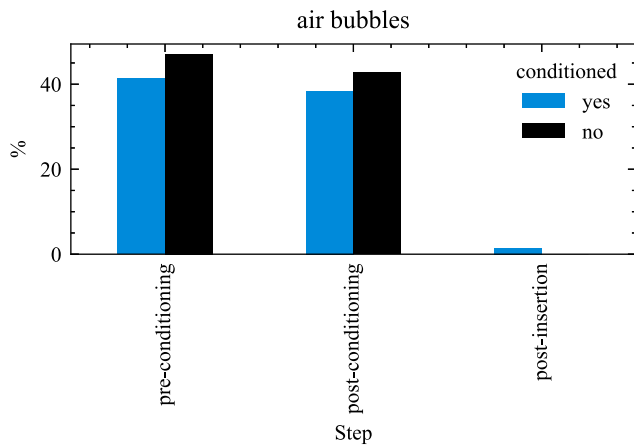
Fig. 5. Comparison of air bubbles before and after conditioning (steps *pre-conditioning* and *post-conditioning*).

conditioned vs. 0 in the non-conditioned groups, respectively (refer to Fig. 5).

E. ECAP Threshold and Its Reproducibility

The ECAP thresholds were measured when the impedance was not being increased by contact air bubbles (Fig. 6(a)). We averaged the data individually, as previously described in the methods. However, due to the limited number of data points for the individual conditioned electrodes, an electrode-to-electrode comparative ANOVA could not be performed. The comparison of all ECAP thresholds in these categories is shown in Fig. 6(b). We found no statistical nor clinically relevant difference within the ECAP thresholds between both groups.

The measurements of the ECAP thresholds, after CI implantation, were performed twice to generate a test-retest accuracy. This allowed for the analysis of the test-retest accuracy. The electrode specific results are shown in Fig. 7(a). The test-retest accuracy showed a standard deviation of 1.6 qu for all conditioned electrodes and 2.1 qu for all non-conditioned electrodes (see Fig. 7(b)). We found that the reproducibility in both groups were not different (F-test; p = 0.2). However, on average, the retest had a consistently higher threshold compared to the test.

IV. DISCUSSION

Determining the electrode impedance is the most important measurement to check the functionality of a cochlear implant. The assessment of the intraoperative impedance measurements requires a high level of experience from the audiologist performing the procedure. In the following, we would like to highlight some factors that we believe can influence electrode impedance.

A. Impedances

Factors influencing impedance: This investigation quantified the electrode contact impedance as a single value in Ohm, which is in concept a very simplistic way to describe the electrode-to-tissue interface [24], [25]. To better describe this interaction is to use the complex impedance spectroscopy [26],

[27], [28], [29], which uses voltage of different frequencies to independently measure the resistive and capacitive components that comprise impedance. Along these lines, it is also useful to utilize circuit models for electrode-electrolyte interfaces, either separately or in conjunction with the complex impedance spectroscopy. However, due to regulatory issues, we used the standard test protocol provided by the manufacturer. The measurement is carried out by performing a stimulation pulse, using a specified current, whilst recording the voltage during the execution of one of its phases. Previous publications have suggested to separate the resistive and capacitive components of the impedance by repeating the measurement several times during a stimulation pulse phase [19]. Moreover, the resistive and capacitive components of the impedance have been previously correlated with different processes (e.g. inflammation, ossification, tissue growth...) within the cochlea [30]. However, this method has yet to become clinically available.

There are several factors that can either separately or altogether influence the overall impedance of the CI electrode contacts. These factors include:

- *Materials [31], [32], [33]:* All intracochlear CI electrode contacts are made of platinum. The reference contacts on the implant housing are made of platinum-iridium (10% iridium). Platinum is known to not have the best electrical properties for biopotential recording electrodes [34], as it is highly polarizable which is needed for stimulation. This causes the electrodes to be more susceptible for motion artifacts.
- *Foreign body reactions:* Inflammation and glia cell formation [35] are too slow to play any role during surgery, however, can play a critical role during the aftercare. Despite the delayed response, insertion trauma is an important factor for adverse tissue reaction [36], [37].
- *Ossification:* (possibly caused by bacterial infection or trauma like temporal bone fracture) [15] is unlikely to occur acutely during CI surgery.
- *Adhering molecules and impurities:* Proteins that adhere to electrode surfaces play a prominent role after implantation [2]. Newbold et al. [38] described changes in biphasic electrode impedance with protein adsorption and cell growth. Furthermore, Tykocinski et al. [19] hypothesized that protein layer appears to form on the electrode surface within the early phase of CI implantation. However, electrical stimulation appeared to disperse this layer of protein, thereby reducing electrode impedance.
- *Anatomical geometry, tissue resistance, and electrode placement:* A previous investigation measured the specific electrical resistance within body tissues [39]. Along these lines, Ellis [40] further describes a more in-depth human body-composition analysis.
- It is sometimes that *lubricants*, such as hyaluronic acid – Healon, oxycellulose – hydroxypropyl methylcellulose, and glycerin, are used during CI surgery for an atraumatic insertion. While Healon and oxycellulose have similar impedance as saline, the impedance glycerin is more than 10 times higher [41]. Lubricants were not used during the investigation.
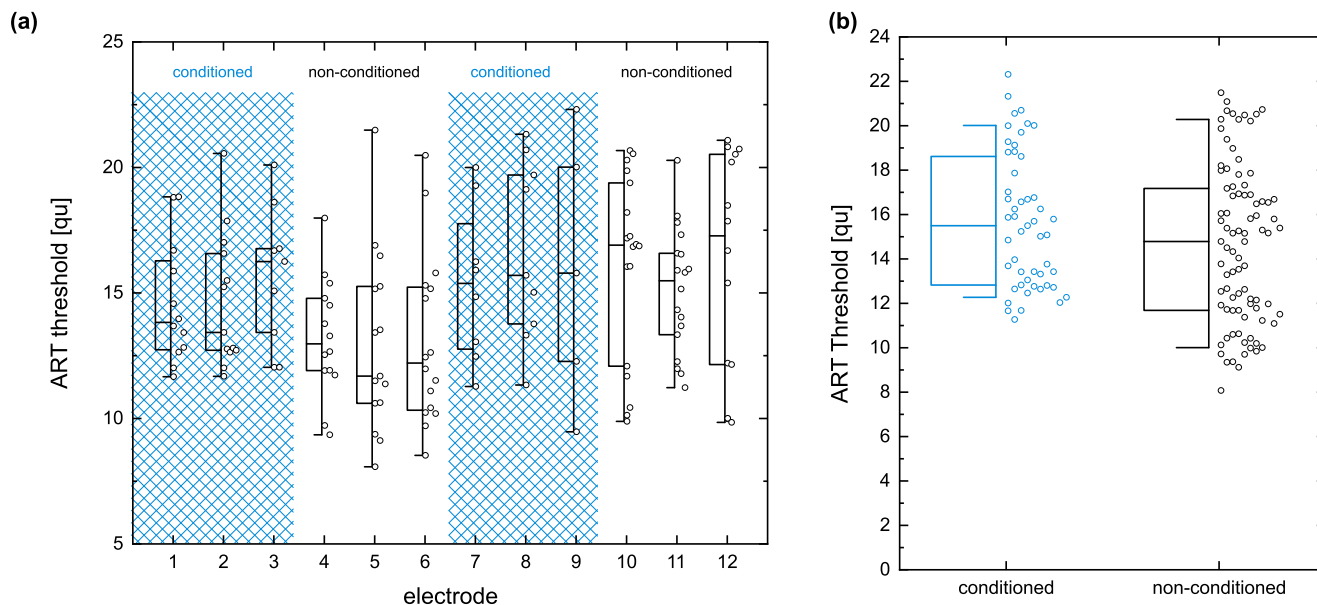
(a)   **(b)**

Fig. 6.   Left: Boxplot of electrode-wise ECAP threshold comparison of conditioned and non-conditioned groups. Median with first and third quartile, whisker showing 10–90 percent percentile as well as raw data are shown. Right: Boxplot with raw data for ECAP threshold comparison of conditioned and non-conditioned electrodes. T-test shows no statistical difference (p = 0.07) between both groups.
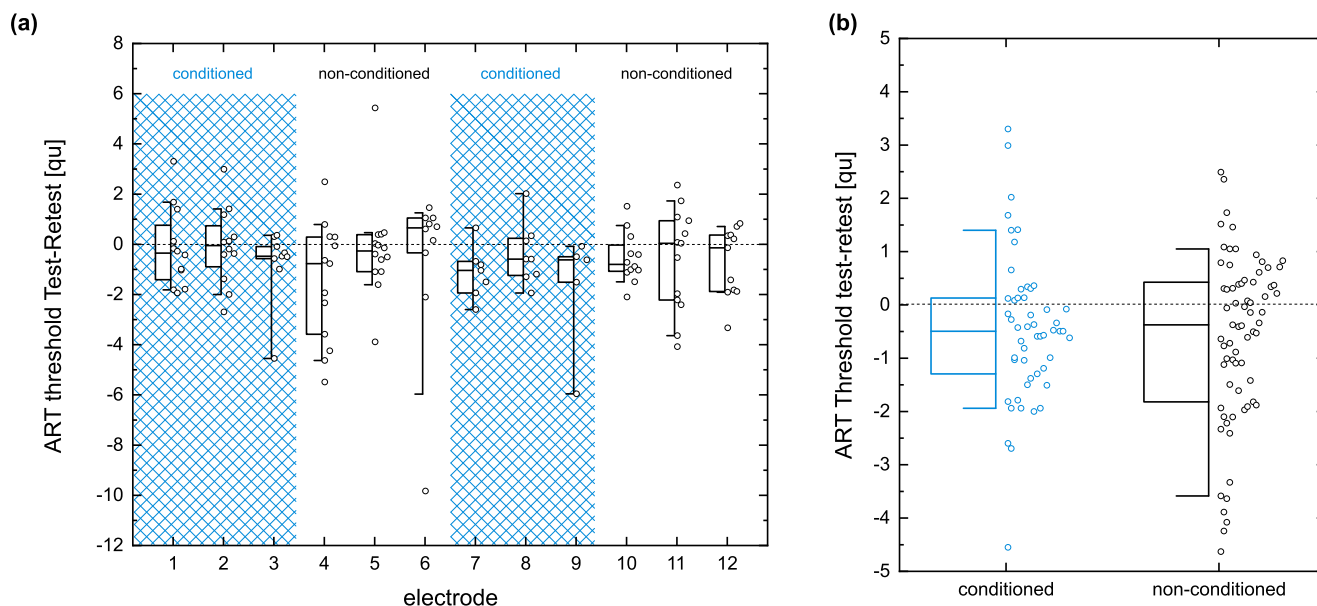
(a)   **(b)**

Fig. 7.   Left: Boxplot with raw data of electrode wise ECAP threshold test-retest comparison of conditioned and non-conditioned groups. Right: Boxplot with raw data for ECAP threshold test-retest comparison of conditioned and non-conditioned electrodes. T-test shows no statistical difference (p = 0.6) between both groups.

- The effects of currents close to or above electrical safety [3], [31], [42] and the effects of non-charge-balanced pulses [36] are not applicable for the current investigation.

It should be noted that we are concurrently measuring two interfaces: (1) the intra-cochlear contact interface; and (2) the larger reference contact interface.

Conditioning effect in CIs: Surprisingly, there have been very few publications describing the conditioning process of CI

electrodes; albeit this concept has been often used. Seminal work of Hochmair-Desoyer (1979) utilized a "stabilization" procedure involving 5 hours of stimulation with 300 Hz pulses applying 4 V amplitude at a 0.3 ms pulse duration [43]. This "stabilization" procedure was applied prior to using the methodology described by Brummer and Turner, which determines the real electrode contact surface area [44].

When analyzing the reduction in impedance after the conditioning of Cochlear's electrode contacts during surgery,

Müller-Deile [9] found that conditioning was relevant for AutoNRT (automated detection algorithm for ECAP threshold) and significantly reduced the measurement time. Furthermore, the reduction in impedance, via conditioning, was exponential in nature, for which there was a linear correlation between the amplitude of the conditioning stimulus and the maximum impedance reduction. For stimulation rates higher than 1200 pps the effect of impedance reduction is no longer rate-dependent. The recommended conditioning amplitude is, however, high whilst low enough allowing the CI to realize the amplitude, given the intraoperative impedances. Ultimately, leading to the suggestion of using 230 "stimulus units" (1.1 mA). The suggested conditioning duration is "as long as the reduction in impedance is no larger than 5%".

Christov et al. [45] argued that the change in impedance and ECAP thresholds, that were observed during surgery, are most likely caused by "electrochemical cleaning" of the platinum-iridium electrode contacts. A detailed in-situ analysis of electrochemical effects on platinum electrode surfaces was performed by Doering and colleagues [46], although they used pulse phase durations in the order of seconds which are much higher compared to the values typically used by CIs.

We observed a 31% reduction in impedance after conditioning within the saline solution. After implantation, between the *post-insertion* and *final* steps, the impedance dropped by 8% for the conditioned group and by 13% for the non-conditioned group. The stimulation pulses needed for the ECAP recordings were acting as conditioning pulses. The first ECAP recording (*AutoART test*) reduced the impedance by 6% (conditioned) vs. 11% (non-conditioned), respectively. Thereafter, the reduction in impedance, caused by the stimulation pulses of the *AutoART retest* (2% vs. 3%, respectively), were already below the previously defined criteria of 5% [9] for *both* groups. This implies that one AutoART recording could be considered "sufficient conditioning" within the given criteria.

Pre- vs. post-insertion: Surprisingly, we did not see an effect of conditioning in regard to a reduction in impedance after implantation. Numerically, the conditioned group even had a higher impedance compared to the non-conditioned group (Fig. 3). The evaluation of the impedances per electrode revealed that, after implantation, the apical contacts 1 to 4 had the highest impedances. This suggests a geometrical interpretation, whereby the diameter of the scala tympani in the apical part of the cochlea is narrower and therefore the impedance is likely higher. During the *post-insertion* step, it was statistically confirmed that contacts 1 to 3 had a higher impedance compared to contacts 7 to 9, all within the same (conditioned) group. We assume that the intrinsic differences in impedance levels were actually due to the electrode contacts along the array, after being inserted in the cochlea, rather than due to the conditioning. Along these lines, we should have randomized the selection of conditioned and non-conditioned electrode contacts between participants.

Impedance comparisons with previous studies: When dissecting previous research, albeit none of the studies performed statistical tests, we found contrasting values in the levels of impedance at the apical point in the cochlea. A graphical comparison of the investigations in Fig. 8 shows studies reporting
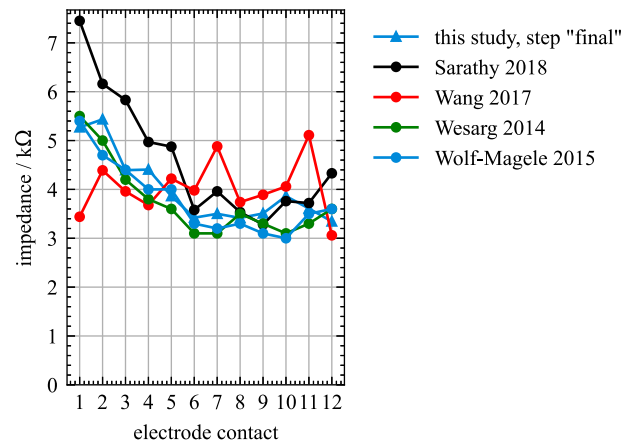

Fig. 8. Comparison of intraoperative impedance values from this and other studies.

either similar [47] or higher [6], [14], [48] levels of impedance from apex to base. Wang et al. [47] reported that the intraoperative mean impedance value in a participant group with a round window membrane CI insertion (35 MED-EL participants with Standard electrode arrays) was 4.03 ± 0.87 kΩ. However, we found that the electrode arrays used in this study consisted of double contacts, which differs from the single contacts used in the current study. Similar to the results of the current study, Wesarg et al. [48] found that the apical contacts indeed had a higher impedance level compared to the other regions of the cochlea when using MED-EL electrode arrays. This finding was further substantiated in the investigations of Wolf-Magele et al. [6] using 45 adult participants and Sarathy et al. [14] in 10 pediatric (2–6 years of age) participants, both using MED-EL electrode arrays.

Impedances of other types of implants, such as those described by Hu et al. [49], are not directly comparable as the electrode array length is typically shorter compared to arrays used in the current investigation.

Reference vs. intra-cochlear contacts: All intra-cochlear electrode contacts share a common reference contact within the implant housing. The reference contacts are constructed of platinum-iridium (10% iridium) vs. the intra-cochlear electrode contacts (surgical grade platinum). Moreover, vast differences between the contacts lie within the surface areas, whereby the reference contact has a surface area of 50 mm^2 [50] compared to the much smaller surfaces of the intracochlear electrode contacts. We found that the conditioning did indeed affect the reference contact alongside the other electrode contacts, which is part of the signal path, in the non-conditioned group. However, since any changes in impedance were mainly seen within the conditioned group, it seems that the effect of conditioning mainly is relevant for the intra-cochlear electrode contacts; given that the impedance reduction was 1.3 kΩ in the conditioned vs. 0.2 kΩ in the non-conditioned group. We estimated that the reduction in impedance within the reference contact contributed to 16% of the total reduction in impedance during *conditioning*, calculated

by dividing the impedance differences in the non-conditioned group by the conditioned group.

Air bubbles: Anecdotally it is speculated that the stimulation of electrode contacts accelerates the dissolution of air bubbles, resulting in a normal impedance. Nonetheless, despite this speculation, we observed that the conditioned group had indeed more air bubbles compared to the non-conditioned group (Fig. 5). Goehring et al. [51], upon analyses of CI impedance abnormalities, found that air bubbles may play a role in both intra- and post-operative abnormalities in electrode impedance. It was assumed the high electrode impedance that occurred during the intraoperative phase only to become normal during the postoperative phase was perhaps due to air bubbles. Along these lines, only 1.6% of the electrode contacts experienced longer time of air bubbles (averaged over different vendors and types of CIs).

B. ECAPs

One method to describe the accuracy of the amplitude (defined as difference between negative and positive peak (N1P1)) of a given ECAP is by using single point error estimation [52]. They demonstrated that an accurate N1P1 amplitude can be assessed from raw data and does not depend on the stimulation level. In the current study the test-retest-accuracy was not evaluated for the measurement of a single ECAP curve, but was extrapolation from an evoked potential thresholds within a set of intensity dependent measurements [53], [54]. However, since the accuracy of the N1P1 amplitude does not depend on the stimulation level it could be assumed that the extrapolated ECAP threshold is an adequate approach for characterizing the quality of the electrophysiological intensity dependent measurements [52]. The comparison of ECAP thresholds for the conditioned vs. non-conditioned electrodes was one of the primary outcome measures for the current investigation. However, the pre-implantation conditioning of CI electrodes within the saline solution showed to have no effect on the ECAP thresholds.

The repeated measurements of the ECAP thresholds under the same conditions offered the possibility to estimate its test-retest reproducibility. The test-retest reproducibility for the conditioned electrodes was approximately within the range of 1.6 qu versus 2.1 qu within the non-conditioned group. However, none of the differences for the test-retest reproducibility were statistically significant. The findings for the stable ECAP threshold were in contrast to the findings of Müller-Deile [9], who showed a significant lowering of the ECAP threshold after re-test following electrode conditioning.

V. CONCLUSION

Although electrode impedance decreased by 31% after conditioning within the saline solution, the impedances of both conditioned as well as non-conditioned groups showed no clinically relevant difference after implantation. Therefore, we saw no clear advantages in conditioning when compared to the non-conditioned group; further, that pre-implantation conditioning would be considered unwarranted. We found that a single run of AutoART reduced the impedances of the implanted non-conditioned electrode contacts by 11%, with the second run reducing impedances by 3% which we do not consider relevant. Thus, AutoART can be interpreted as a method of "in-vivo conditioning", albeit this does not result in a relatively differing ECAP threshold.

The reduction in impedance of the reference electrode contributed to approximately 16% of the total impedance reduction via conditioning. Therefore, we determined that the more important effects actually occur on the electrode array. However, we found that the conceptualization of removing air bubbles thru electrical stimulation did not work.

It appears that shipping and non-usage of the CIs for weeks and months shows no negative influence on intraoperative ECAP threshold measurements and its reproducibility. In summary, pre-implantation conditioning for this type of MED-EL CI electrodes appears to not be a necessity.

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