Aus der Klinik für Hals-Nasen-Ohrenheilkunde, Kopf- und Halschirurgie im
Klinikum Bielefeld Mitte

DISSERTATION

“ Elektrophysiologische Effekte der slim straight intracochlearen Elektrodenposition ”

“Effect of slim straight intracochlear electrode position on neural response thresholds”

zur Erlangung des akademischen Grades
Doctor medicinae (Dr. med.)

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1. Abstrakt

1.1. Abstrakt (Deutsch)

Einleitung: Cochleaimplantate ist die Behandlung der Wahl für Patienten mit hoch bis schwergradiger Innenohrschwerhörigkeit, die noch Resthörvermögen haben. Die elektrische Stromverteilung innerhalb der Cochlea durch eine Cochlea-Implantatelektrode ist für eine optimale postoperative Hörleistung entscheidend. Eine Slim Straight Elektrode ermöglicht die Platzierung der Elektrodenkontakte in lateraler oder medialer Richtung zum Modiolus. Die elektrophysiologische Wirkung dieser unterschiedlichen Kontaktrichtungen erscheint bisher unbekannt.

Studienziel: Das Ziel dieser Studie war es, den Einfluss der intracochlearen lateralen oder medialen Elektrodenplatzierung auf das elektrophysiologische Verhalten zu untersuchen.

Studiendesign: Retrospektive klinisch und deskriptiv experimentelle
Studienort: überregionales Krankenhaus der Maximalversorgung.

Material und Methoden: Eine slim-straight Elektrode wurde in die Cochlea von fünf Patienten (zwei weibliche und drei männliche) eingeführt und die daraus resultierende Neural Response Thresholds (NRT's) in lateral sowie medial ausgerichteter Kontaktposition gemessen. Außerdem erfolgte einer in-vitro Untersuchung der Cochlea (de-capping) aus dem Felsenbein von insgesamt fünf Spendern. So konnte die Insertionsverhalten der jeweiligen Elektrodenkontaktposition (lateral gegenüber medial) beobachtet / ausgewertet werden.

Ergebnisse: Es zeigten sich keine signifikante Unterschiede in den NRT's zwischen der lateralen und der medialen Position der Elektrodenkontakte. Die in-vitro Felsenbeinstudie konnte kein intracochleares Torsionsverhalten der Elektrode innerhalb der lateralen oder medialen Positionierung nachweisen.

Fazit: Die Ergebnisse deuten darauf hin, dass die intracochleare Position von Slim Straight Elektroden die NRT's nicht beeinflusst.

1.2. Abstract (English)

Introduction: Cochlear implantation is the treatment of choice for patients with profound-to-severe sensorineural hearing loss who retain residual hearing. The electrical current distribution of a cochlear implant electrode array is essential for an optimal postoperative hearing benefit. Placement of an electrode contact in a lateral or medial direction to the modiolus is possible with a slim straight electrode design. The electrophysiological effect of this different contact position appears to be unknown.

Objective: Our goal is to investigate the electrophysiological effects with different intracochlear electrode contact positions.

Study design: Retrospective clinical and descriptive experimental
Setting: Tertiary referral center.

Material and Methods: A slim straight electrode was inserted into the cochleae of five patients (two female and three male) and the neural response thresholds (NRT's) were measured in a lateral and medial directed contact position. Additionally, the cochleae in five temporal cadaveric bones were de-capped to allow for in-vitro direct observation of the inserted slim straight electrode contact position, either in a lateral versus medial position.

Results: There was no significant difference in NRT's between lateral versus medial contact position. While the in-vitro temporal bone study indicated no intracochlear torsion behaviour within the lateral or medial electrode contact position.

Conclusion: Our results suggest that the intracochlear positioning of a slim straight electrode does not affect NRT's.

2. Mantentext

2.1. Introduction

In 1961 the first Cochlear implantation of a single-channel electrode through the round window was performed by William (Bill) House and John Doyle in Los Angeles, California. Later on, in 1963, the German otologist Zöllner, formulated the basic principles of intracochlear multichannel stimulation, which is the base of today's cochlear implant systems. In 1964 Blair Simmons and Robert White from Stanford University placed a 6-channel electrode. The following stage was a clinical trial on a cohort of patients. Robin Michelson, Robert Schindler, and Michael Merzenich at the University of California, San Francisco, led these experiments in 1970 and 1971. The last phase in the establishment of Cochlear implantation involved the evaluation of implant users. This was a request from the National Institutes of Health and was published in 1977 by Robert Bilger and coworkers at the University of Pittsburgh, Pittsburgh, Pennsylvania. By the end of 1980 after the establishment of clinical feasibility for Cochlear implantation, as well as the commercialization of the technology, became the leading treatment for profound deafness in the United States, Europe, and Australia [1].

The Cochlear Implant is the successful achievement of an electrical stimulus in the ear to reproduce sound. A Cochlea Implant is a device that converts sound in to an electrical current that is able to stimulate hearing. There are up to twenty contacts within the electode stimulating the scala tympani to reach tonotopy simulation through different stimulus modalities [2].

With over 324,000 cochlear implants (CI) performed worldwide, cochlear implantation is the treatment of choice for patients with profound-to-severe sensorineural hearing loss (SNHL) who retain residual hearing[3]. The cochlear implant electrode is a central component of the implant–neuron interface. Its design and location play an important role in the preservation of residual hearing, intracochlear electrophysiological behavior, and speech comprehension [3,4,5,6,7].

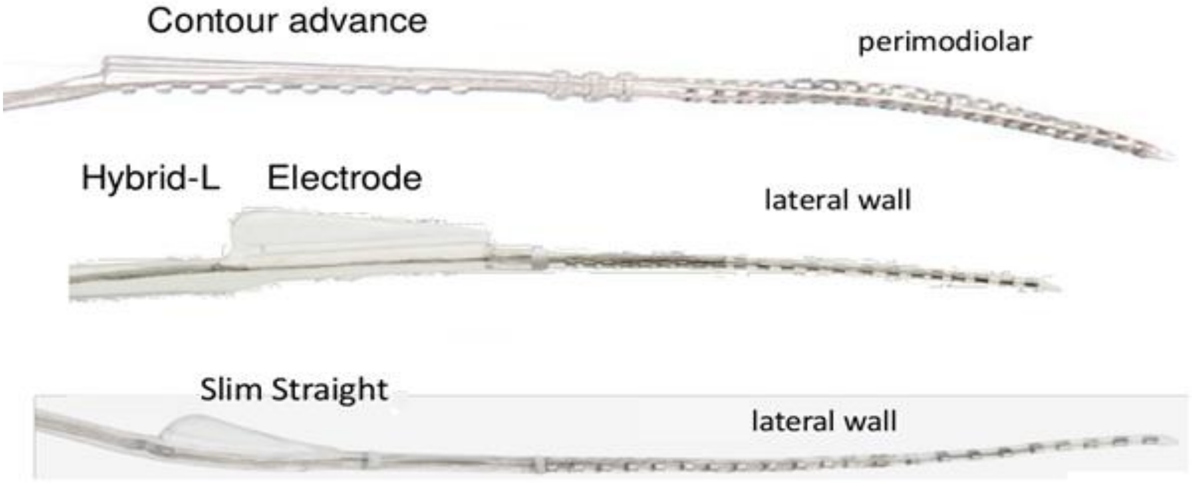
The performance of individuals with a cochlear implant can vary to a great extent. One of the many parameters that can affect its performance is the presentation of an electrical stimulation from the cochlear implant to the auditory nerve. The activity of the auditory pathways can be recorded by evoked potentials. Electrical evoked potential is a response to multiple electrical impulses generated by the auditory nerve [8].

To achieve an optimal hearing benefit with a cochlea implant, the electrode positioning within the scala tympani is crucial. Placement of the cochlear implant electrode within the scala vestibuli is correlated with worse audiological outcomes[9]. The intracochlear position of the electrode can result in different nerve stimulus, modifying the transmission of pitches perceptions. Which is the base for speech understanding following cochlear implantion[2]. Several physiological and anatomical factors are important to consider; such as cochlear size, intracochlear fibrosis, local vascular lesions, intracochlear hemorrhage, inner ear fluid leakage and/or hair cell death can deteriorate the quality of the interface between the electrode and the auditory nerve endings[10].

Current cochlear implant systems are partially implantable and equipped with a multitude of additional functions. Similar to hearing aids for sound pre-processing and noise elimination[2]. There are also different electrode designs focusing on different current distribution and hearing preservation. This have led to the development of three main types of electrodes: perimodiolar, midmodiolar and lateral wall electrodes.
(Figure 1.)

Figure 1: (source:Cochlear Ltd. Sydney).

1a) Types of electrodes



1b) Intracochlear view

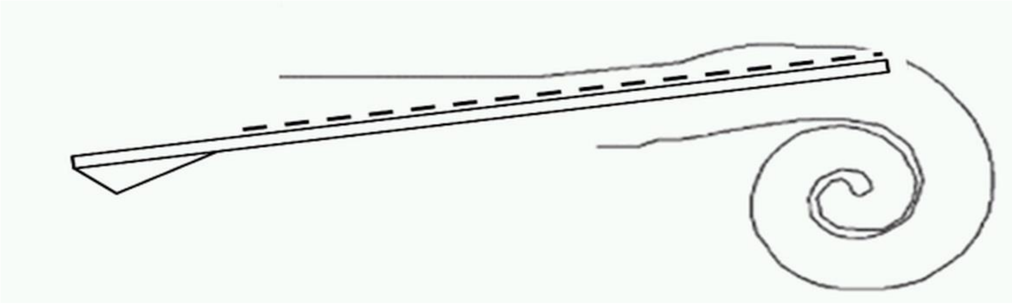
The electrically evoked compound action potential (ECAP) were first measured in cochlear implant (CI) recipients in 1990. ECAP action potential measurement capabilities (termed neural response telemetry or NRT) have been included in the Nucleus implant by Cochlear Ltd. since 1998 (Sydney, Australia). The neural function of the inner ear can be contingent from the evoked compound action potential, representing a synchronous neural firing at the stimulus onset. The auditory nerve neurophonic (ANN) represents a locked firing neural phase over the duration of a tone. The auditory nerve neurophonic is only seen with alternating phase tones. This can appear as a sinusoidal waveform with twice the stimulus frequency when using the standard NRT recording system, since this is peripheral, and an objective measurement of the electrical response by the auditory system[11,12].

The design of perimodiolar and midmodiolar electrodes are concentrated on the intracochlear current distribution. Showing that a position close to the modiolus can led to lower neural response thresholds, induced minor spread of electrical current and less interference between the channels[13,14,15]. In contrast, lateral wall electrodes were developed to preserve residual hearing. However, the disadvantages of using these electrodes are higher neural response threshold levels and a higher risk of facial nerve stimulation[14,16]. Lateral wall electrodes were designed with a contact to one side and a wing to the contralateral side, guiding the contact to the side of the modiolus (slim straight lateral). It is assumed that this design helped guide the current spread in the direction of the modiolus with less electrode rigidity. Since the wing of the electrode is on the contralateral side were the electrode contacts, a right-handed surgeon [as most surgeons are (75–95 per cent)] will regularly insert this kind of electrode in a right ear with the contacts in the direction of the modiolus[17]. When using the wing to hold the electrode in a left ear with the right hand, the surgeon will place the contacts away from the modiolus. These laterally positioned contacts might potentially lead to higher neural response thresholds with possible effects on stimulus levels, spread of excitation, canal interaction and consumption power. (Figure 2.)

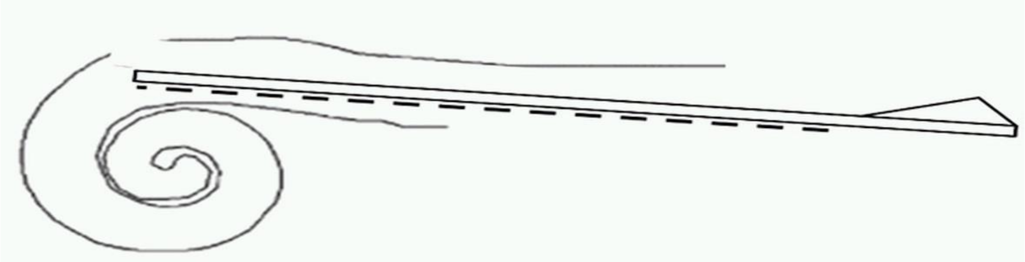
Figure 2: Slim lateral electrode diagrams showing position of contacts and wing

(source: own illustration)

2a) Right ear



2b) Left ear



Intraoperative, this implant allows for enhanced functional control through electrophysiological analysis to asses and evaluate the CI devise integrity. Also, to confirm correct intracochlear position of the electrode array, and allow system adjustments.Especially in children, based on objective parameters. The subsequent hearing and speech training is targeted at speech acquisition and recognition. The long-term follow-up involves also technological upgrades and the treatment of complications beside medical and technical controls [2,11].

Our goal is to investigate the electrophysiological effects with different intracochlear electrode contact positions, either medial or lateral.

2.2. Materials and Methods

In this retrospective clinical and descriptive experimental study a total of five patients were included. Three cases had sudden hearing loss, one case noise trauma, one unknown case. From all patients electrophysiological measurements were performed, initial in a lateral (Group 1) and subsequently in a medial (Group 2) contact position. Our inclusion criteria involved implanted patients with the Nucleus slim straight electrode developed by Cochlear Ltd. (product 522-Figure 3). A thin diameter softip with apical flexibility and smooth lateral wall surface facilitates an easy single stroke insertion. The design is to protect the delicate cochlear structures, and has demonstrated to be useful in low-frequency hearing preservation.

Characteristics: (Cochlear Ltd.-Sydney)

1. A 0.3mm softip diameter at the apex minimizes insertion trauma
2. 22 half-banded platinum electrodes delivers the greatest number of spectral channels over 19.1 mm active length
3. Intracochlear electrode has a smooth lateral surface
4. The two white markers indicate insertion depth at 20 - 25 mm.
5. Patented basal stiffener, enables a smooth and single motion insertion for ease use while minimizing trauma
6. Basal diameter is 0.6 mm
7. Handle and optimized lead angle aids in electrode orientation and surgical handling
8. The two extracochlear electrodes are designed to deliver a more individualized stimulation and better mapping
9. The slim straight electrode is suitable for round window or cochleostomy procedures
10. Power efficient
    a. Stimulus amplitude range: 0 to 1.75 mA
    b. Stimulation rates up to 31.5 kHz
11. Implant identification
12. Stimulation modes
    a. Monopolar and bipolar ground stimulation modes uses biphasic currency pulses

13. Telemetry capable
    a. Ultra-low-noise floor (approx. 1 uV) enables advance AutoNRT telemetry capabilities
    b. Includes fully integrated electrophysiologic telemetry modes: NRT, AutoNRT, ESRT, ABR, CEP and intraoperative NRT

Figure 3. (source:Cochlear Ltd. Sydney): The CI Slim straight Electrode.

Exclusion criteria included cochlear ossification, obliteration, neural deficiencies and residual hearing. All patients underwent implantation between 2017 and 2018 with a standard surgical procedure that included a post-auricular transmastoid approach, a posterior tympanotomy and a round window electrode insertion. Before initial insertion, the electrode was moisturized with a glicocorticois-triamcinolone. After placement of the initial lateral contact position and electrophysiological measurement, the position was changed to a medial contact direction and stimulus was remeasured. Finally, the electrode and the round window were covered with fascia.

This study was reviewed and supported by the institutional review board of Klinikum Bielefeld (approval number: HNO-KLIBI- 08- 2017) and has been conducted according to the principles expressed in the Declaration of Helsinki. The patient gave their written consent to the participation of the study. The Neural response threshold data and temporal bone in-vitro observations data that were used to support the findings of this study are available from the corresponding author upon request.

2.2.1. Temporal bones:

The ENT department at Klinikum Bielefeld Mitte has a temporal bone laboratory, which facilitates the surgical team/staff to practice surgical technique and implant insertion in cadaveric specimens. For our study we received five (three left and two right) temporal bones from cadaveric donors.

In the laboratory these bones were harvested and the cochlea was drilled until fully visualization of the basilar membrane. All of these procedures were carried out under moisturized conditions (0.9% NaCl). The microscope used was the Zeiss OPMI Pentero 900, and the drilling system was the Micro Drill- and Shaver System (DT55) from Spiggle & Theis. All procedures (drilling and electrode insertion) were performed by the same experienced ENT surgeon.

Following, the basilar membrane was removed to allow a better visualization of the electrode and its contact direction. The insertion procedure was microscopically evaluated, and photographs were taken. During the temporal bone analysis, the electrode was always held by the designed wing independently of the procedure, ear side and surgeon's hand (right/left), or other specific situation, for example, when the straight slim electrodes needed to be inserted twice up to 22 mm. In this case the initially insertion was with the contacts laterally directed, followed by the contacts being medially directed. And the second situation would be to check or rule out electrode torsion.

The electrode position was always monitored with digital images; these images were captured by the Karl Storz's AIDA documentation system connected to the microscope. Finally, all procedures and in-vitro observations were performed on different days, since the drilling of the temporal bones lasted several weeks.

2.2.2. Radiologic evaluation

To determine electrode position, a cone beam computed tomography (CT) (NewTom VGI, Verona, Italy) was utilized. The parameters assessed were; field of view, 15 × 15 cm, 10.48 mAs, 20.52 mAs, 110 kV and 360°. The cone beam CT was followed by two-dimensional (2D) and three-dimensional (3D) reconstruction at an external workstation (NNT software, main station). All post-operative radiological images were reviewed by an experienced surgeon and neuroradiologist.

2.2.3. Data acquisition and NRT-evaluation

Neural response thresholds were obtained. Software-based neural response recording thresholds were also used to measure and evaluate the neural response on each sample (Cochlear's Custom Sound® fitting software, version 4.4).

All measurements were recorded twice, in a lateral and medial contact position. The neural response telemetry (NRT) measures electrical evoked compound action potentials (ECAP) when an electrode pulse-stimulus is applied within the intracochlear space. Furthermore, voltage-response measurements will continue on the adjacent electrode until the circuit is complete, and before information is send back to the telemetry receiver system. These electrophysiological thresholds are evaluated visually on a monitor by a clinician measuring the amplitude signals. The Nucleus Freedom Cochlear Implant System allows for manual and/or automatic measurements of neural response telemetry algorithms.[11] All measurements were obtained over different dates due to surgical scheduling. However all surgeries were performed by the same experienced ENT surgeon.

A Microsoft® Excel® spreadsheet (Microsoft® Corp.) was utilized for data entry. Data were statistically analyzed using the StataCorp Statistical software (STATA®) version 13.1 (STATA Statistics/Data Analysis, Texas, USA) and R 4.03 (including the library "blandr") . Mean and standard deviation were calculated for all parameters and the t-test with Boxplots and Bland- Altman plots were used for variables comparison. Significance was adopted at $p < 0.05$ for interpretation of the test results.

2.3. Results

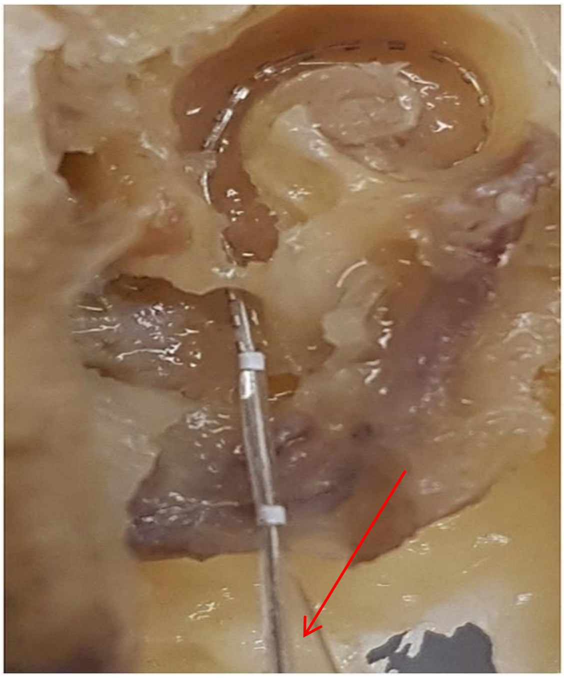
The insertion behavior of the electrodes in the temporal bones was evaluated through a microscope in-vitro observation. The lateral electrode position and medial electrode position were compared (Group 1 versus Group 2). The patients were two female and three male (mean 58 y.o, range 31- 84 y.o). The mean duration of hearing loss was five point six years (range 1 - 20 y.)

2,3.1. Temporal bone in-vitro observations:

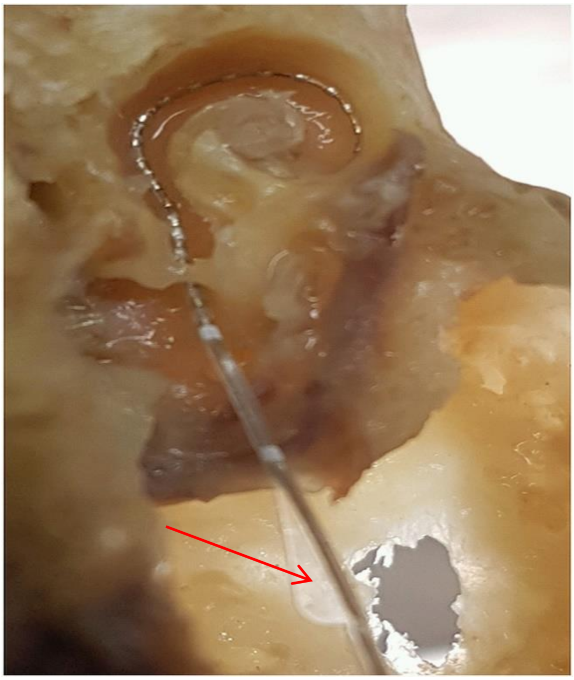
We evaluated five temporal bones with a measured mean ‘A’ distance, (10.45 mm, SD, 0.18)[18]. The intracochlear behavior of the electrode during the insertion showed no relevant torsion in terms of significant changes of contact direction independent of the size of the cochlea. In all cases, a wing directed contralateral direction of the contacts remained stable over the whole electrode length. (Figure 4.)

Figure 4: Images showing temporal bone with an uncapped cochlea and electrode contact position. **(source: own illustration)**

4a) Medial contact position (arrow: lateral wing)



4b) Lateral contact position (arrow: medial wing)

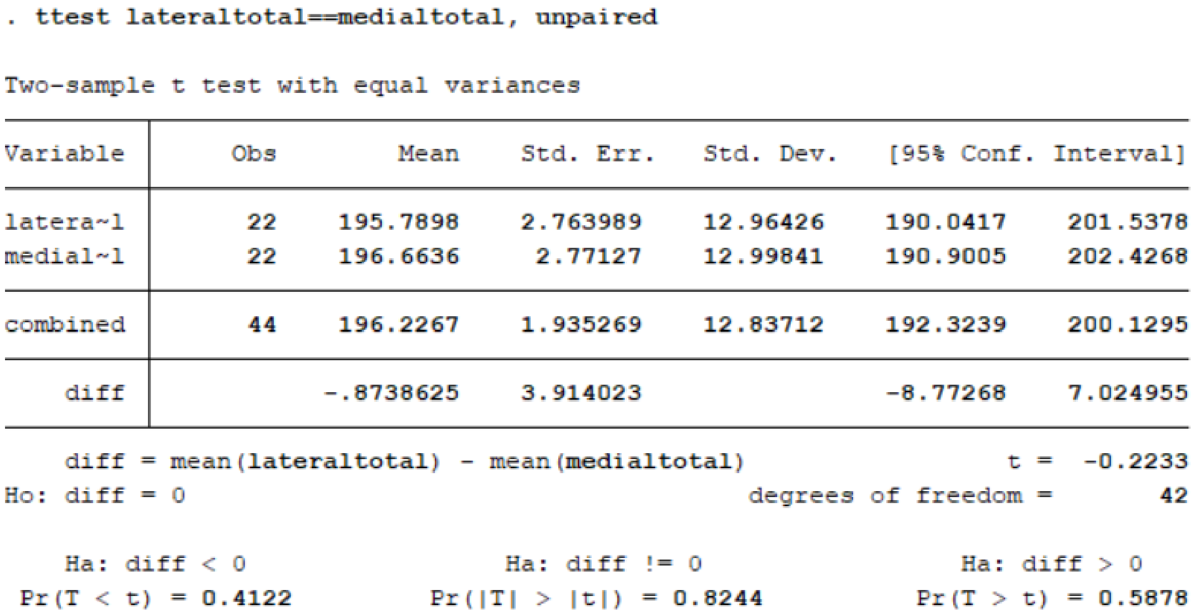


2.3.2. Neural response threshold measurements:

In all cases, we measured the lateral and medial position of the contacts twice. There were no cases where the maximum current unit deviation of a single contact between the lateral and medial position of the contacts was larger than the maximum deviation between first and second neural response threshold measurement. The mean neural response thresholds for lateral and medial position were 195.7 ± 12.9 current units (lateral) and 196.6 ± 12.9 current units (medial).

This difference was not statistically significant: ($p = 0.8244$). (Table 1, Figure 5 and 6)

Table 1: Overall evaluation between total NRT of medial and lateral contact position.



```
. ttest lateraltotal==medialtotal, unpaired

Two-sample t test with equal variances
------------------------------------------------------------------------------
Variable |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
latera~l |      22    195.7898    2.763989    12.96426    190.0417    201.5378
medial~l |      22    196.6636     2.77127    12.99841    190.9005    202.4268
---------+--------------------------------------------------------------------
combined |      44    196.2267    1.935269    12.83712    192.3239    200.1295
---------+--------------------------------------------------------------------
    diff |           -.8738625    3.914023               -8.77268    7.024955
------------------------------------------------------------------------------
    diff = mean(lateraltotal) - mean(medialtotal)                 t =  -0.2233
Ho: diff = 0                                     degrees of freedom =       42

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.4122         Pr(|T| > |t|) = 0.8244          Pr(T > t) = 0.5878
```

(own illustration -STATA® version 13.1)

Figure 5: Boxplot: Electrode contact: Lateral versus Medial Overall

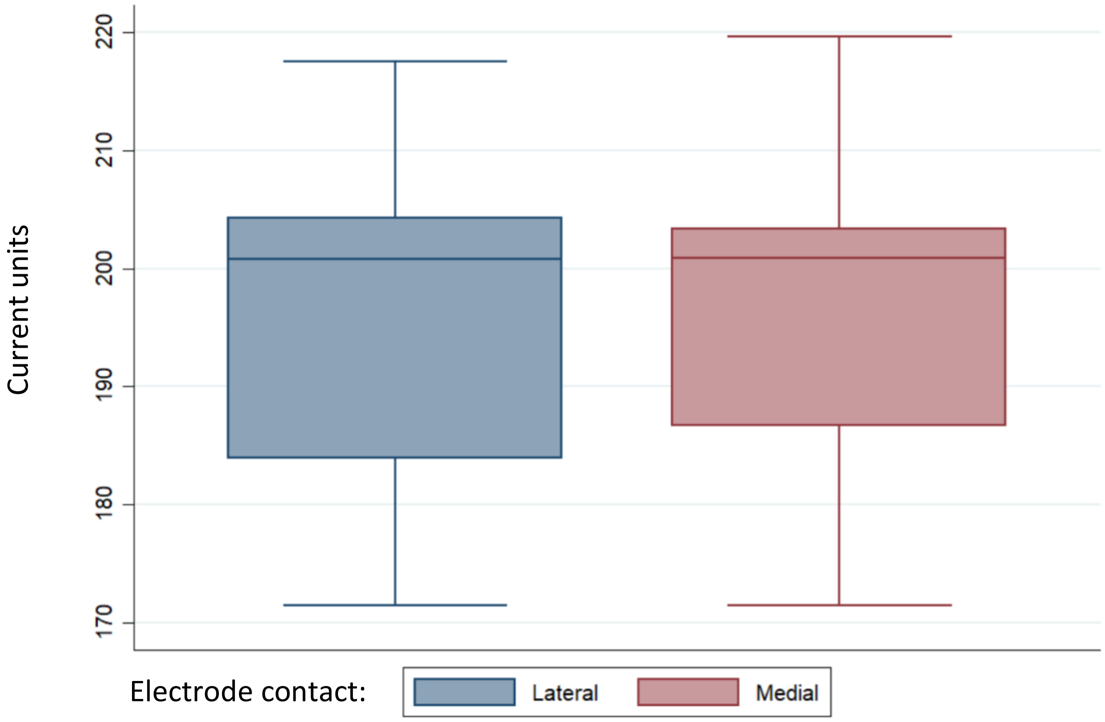


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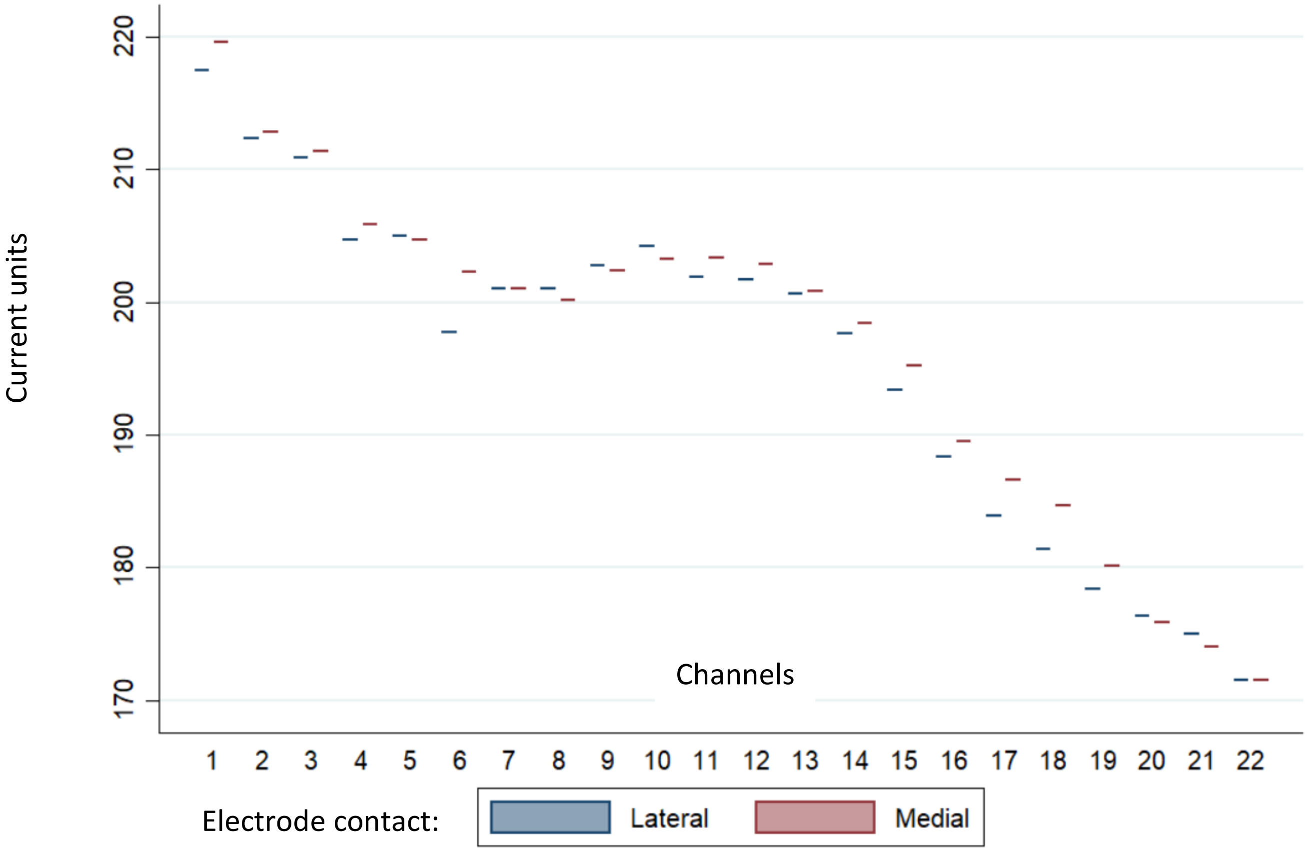
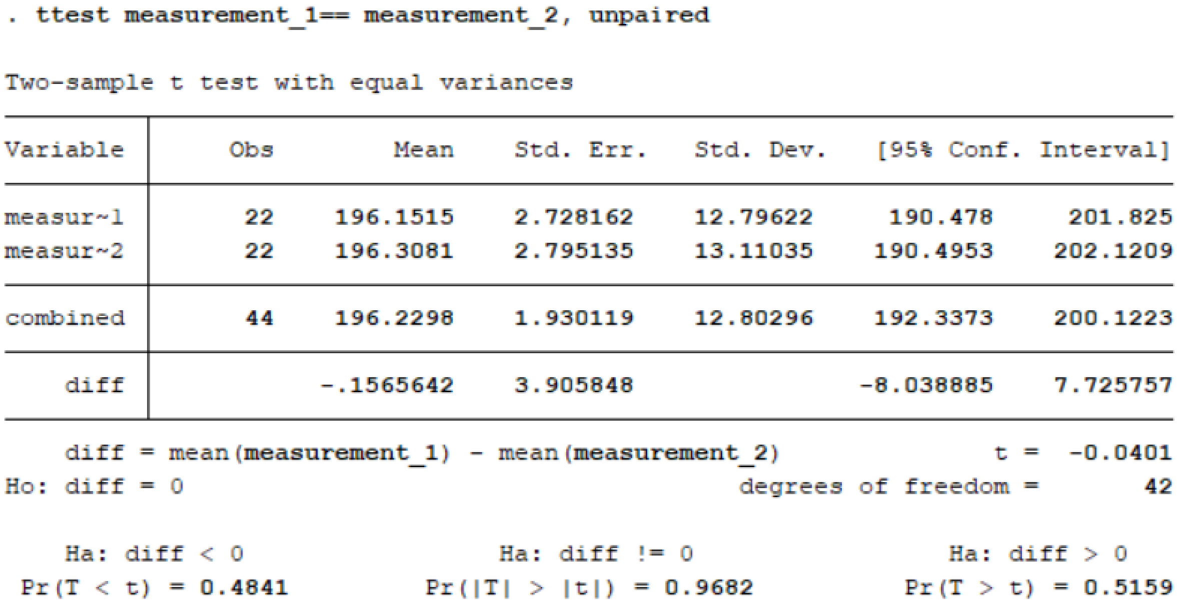
Figure 6: Specific mean values for neural response threshold of medial and lateral contact position by channel.



(own illustration -STATA® version 13.1)

The mean neural response thresholds for the first and second measurement were 196.1 ± 12.8 current units and 196.3 ± 13.1 current units, respectively. This difference was statistically not significant: (p = 0.9682). (Table 2, Figure 7 and 8)

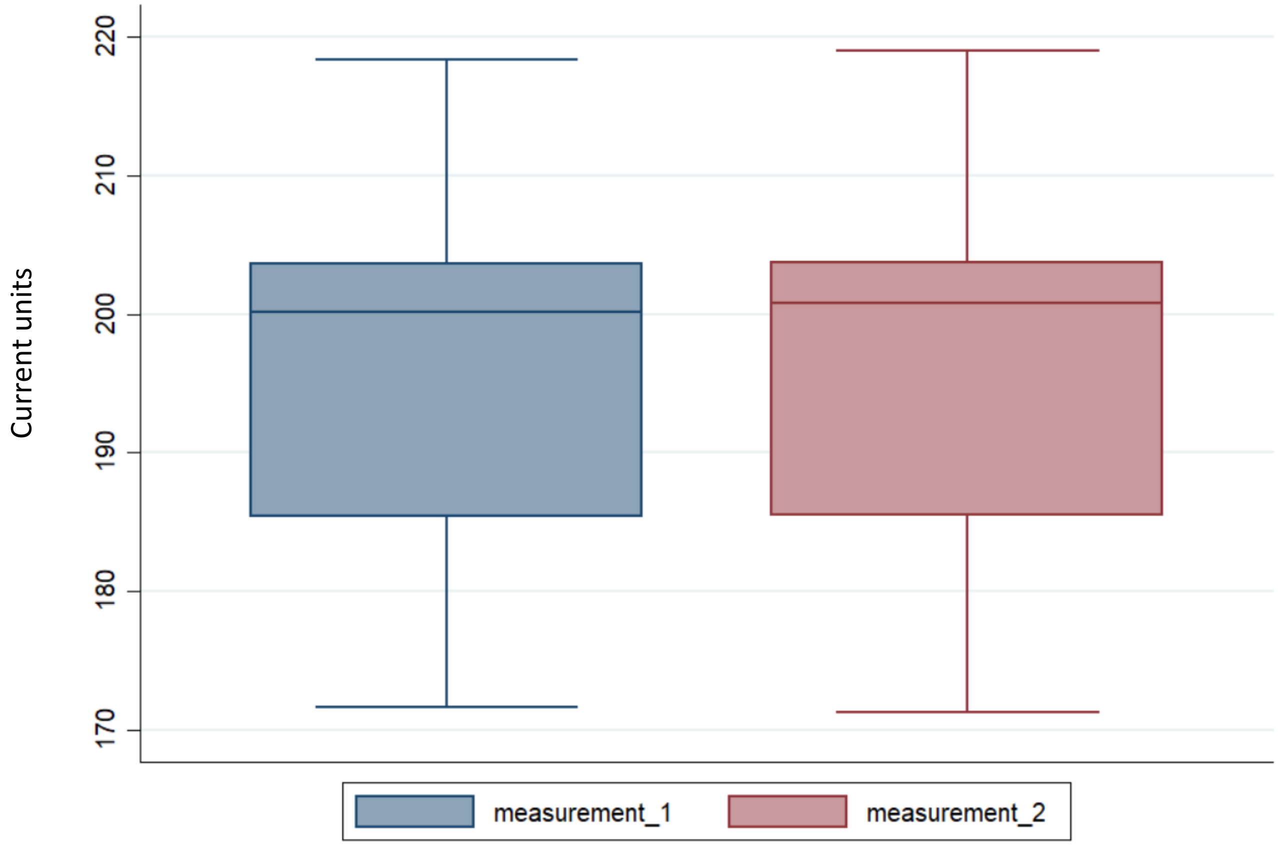
Table 2: Overall evaluation between total NRT of first and second measurement



```
. ttest measurement_1== measurement_2, unpaired

Two-sample t test with equal variances

Variable |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
measur~1 |      22    196.1515    2.728162    12.79622     190.478     201.825
measur~2 |      22    196.3081    2.795135    13.11035    190.4953    202.1209
---------+--------------------------------------------------------------------
combined |      44    196.2298    1.930119    12.80296    192.3373    200.1223
---------+--------------------------------------------------------------------
    diff |           -.1565642    3.905848               -8.038885    7.725757
------------------------------------------------------------------------------
    diff = mean(measurement_1) - mean(measurement_2)              t =  -0.0401
Ho: diff = 0                                     degrees of freedom =       42

    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.4841         Pr(|T| > |t|) = 0.9682          Pr(T > t) = 0.5159
```

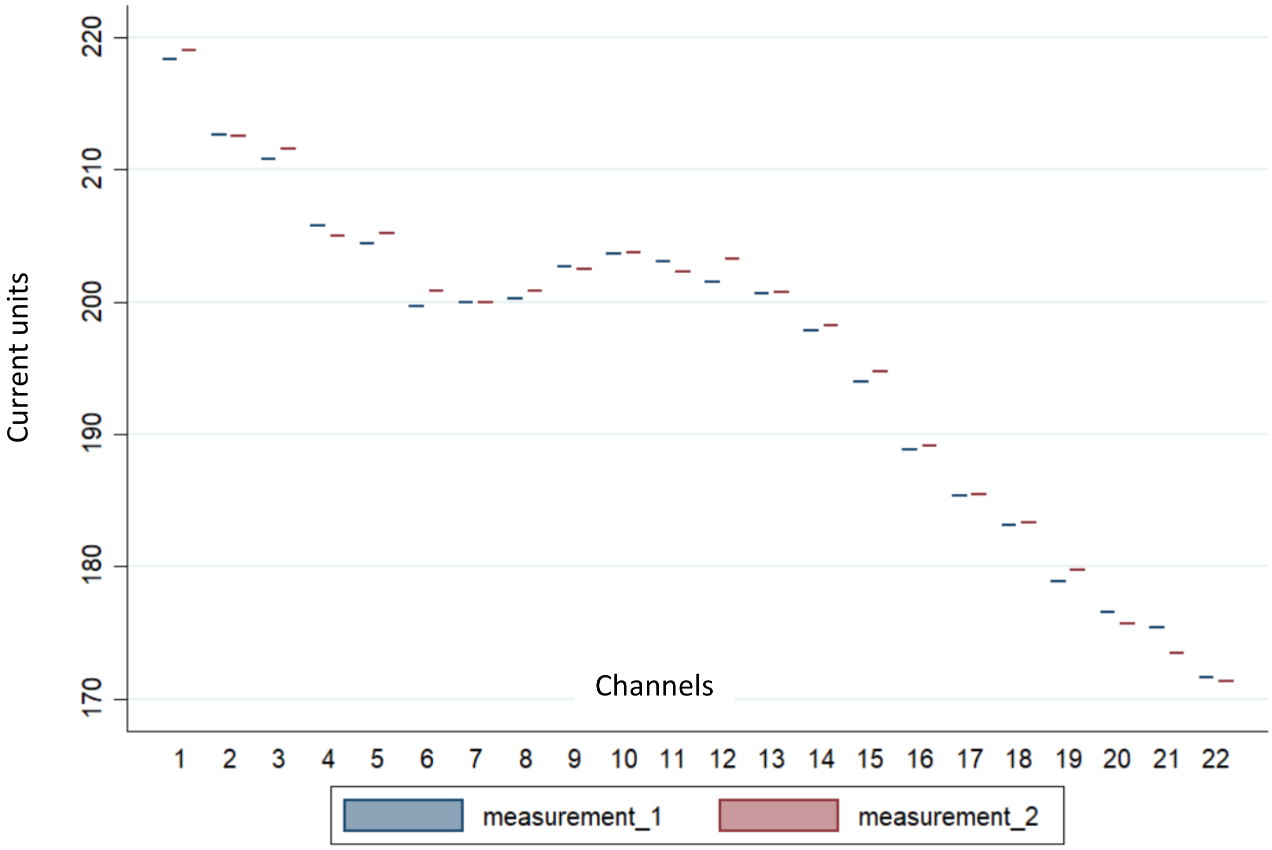
(own illustration -STATA® version 13.1)

Figure 7: Boxplot: Measurement 1 versus Measurement 2 Overall



(own illustration -STATA® version 13.1)

Figure 8: Measurement 1 versus Measurement 2, by Channel



(own illustration -STATA® version 13.1)

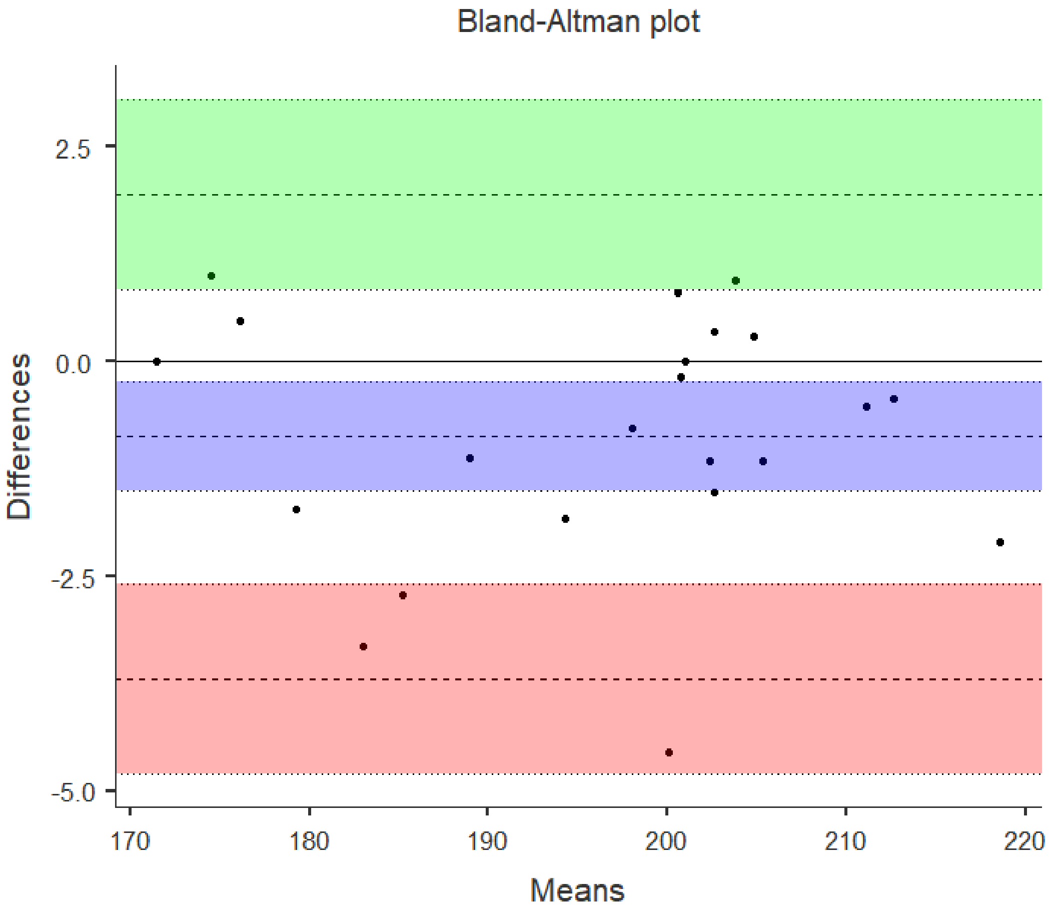
Finally, Bland- Altman plots were performed to statistically validate our hypothesis. Namely, we compared the following variables: electrode contact positions lateral and medial (Fig. 9) as well as measurement 1 compared to measurement 2 (Fig. 10).

The difference from the mean of two variables was estimated as follows: (i) for lateral versus medial: bias -0.87, upper limit of agreement (LOA) = 1.94, lower limit of agreement = -3.69; (ii) for measurement 1 versus measurement 2: bias - 0.15, upper limit of agreement = 1.42, lower limit of agreement = - 1.73.

In both Bland- Altman plots, the majority (95%) of data points were in the middle zone of the diagram (within the range of acceptance of the difference from the mean). This supports our hypothesis inferring that there is no significant difference between lateral or medial electrodes contact position as well as between the measurements 1 and measurement 2, being all these variables analysis comparable to each other.

Figure 9: Bland-Altman plot: Electrode contact: Lateral versus Medial Overall

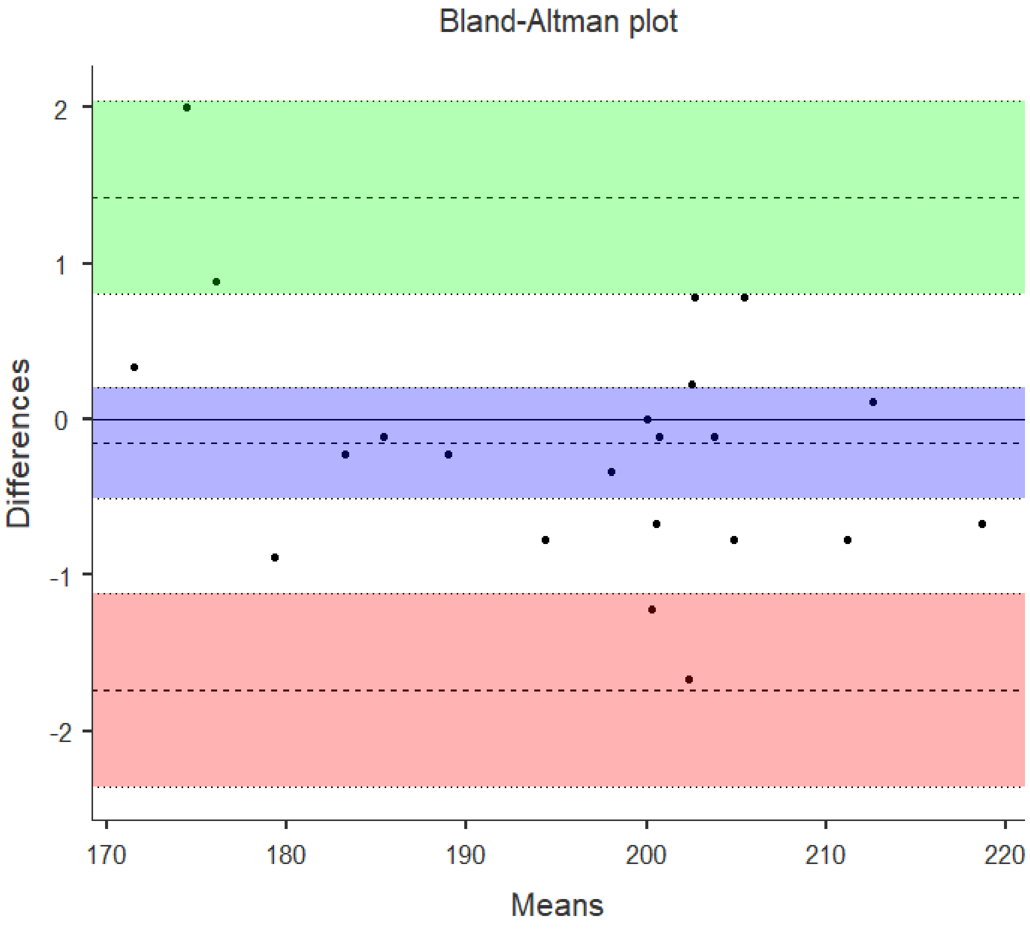
	Estimate	Lower limit of 95% confidence interval	Upper limit of 95% confidence interval
Bias (n = 22)	-0.87	-1.51	-0.24
Lower limit of agreement	-3.69	-4.80	-2.59
Upper limit of agreement	1.94	0.84	3.05



(own illustration -R® version 4.03)

Figure 10: Bland-Altman plot: Measurement 1 versus Measurement 2 Overall

	Estimate	Lower limit of 95% confidence interval	Upper limit of 95% confidence interval
Bias (n=22)	-0.15	-0.51	0.20
Lower limit of agreement	-1.73	-2.68	-1.11
Upper limit of agreement	1.42	0.80	2.04



(own illustration - R® version 4.03)

In all cases a certain scala Tympani position was verified under cone beam CT on postoperative day**.**

2.4. Discussion

Cochlear implantation is a safe and a reliable procedure of choice for the treatment of profound-to-severe sensorineural hearing loss in patients with residual hearing. The round window approach and use of a slim straight electrodes can preserve Cochlear structures and hearing[19]. The position of the electrode array in the cochlea is fundamental for the interaction between the implant and the cochlear neuronal structures because it determines the localization of current stimulation. The therapeutic advantage of the longer electrode is a wider cochlear coverage stimulating the low-frequency region of the cochlea in patients with less preoperative residual hearing or rapidly progressive hearing loss[20]. Other than local neural factors, the electrode position itself is of central importance for the threshold. The neural response threshold ratio is the relative variation of the distance between the electrode array and the spiral ganglion in different cochlear regions[21,22]. In general, lateral wall electrodes are known to cause higher neural response thresholds[14]. Besides an positive effect on speech understanding, which is discussed with straight electrodes, a better pitch-ranking ability and less channel interaction has been shown, as measured with the neural response threshold function trough the interaction of the contact position in this type of electrodes [14,23]. Several studies have shown that electrode contact position is a central factor affecting speech understanding. [6,7,24] . A scalar change and electrode tip folding has been shown to be detectable even by electrophysiological measurements[25,26]. An advantage of this system is the intraoperative identification of electrode glitches, for example, electrode tip fold-over. This problem can be corrected during surgery to avoid pitch errors, vertigo, tinnitus, and/or new bone or fibrous tissue formation at the intra-cochlear site where the electrode tip failed (bending, kinking and tip fold-over)[27].

The placement of a straight electrode within the scala tympani has become the goal standard due to improved design advantages; thinner and more flexible than the more voluminous and stiff pre-contoured electrodes[22]. The optional positive influence on the neural response threshold by a surgical modification has been evidenced by performing a so-called ‘pull back’ of a perimodiolar electrode[28]. Recent evidence suggests that speech discrimination is not improved by deep insertion, but rather improved by perimodiolar position within the Scala tympani or vestibuli[29]. Our goal is not to compare electrode positioning within the scala tympani versus vestibuli, which already has been described. We aim to determine if intracochlear medial or lateral electrode position can result in improved electrophysiology behavior.

After T-test, Boxplots and Bland-Altman plots statistical analysis was performed, we found that the neural response thresholds in either position maintains a similar value without significant alterations, regardless of the direction placement (medial versus lateral). Since no significant difference between the two positions was found, we cannot reject the null hypothesis. Therefore there should be no subsequent greater impact on speech discrimination outcomes.

The manufacturer recommends insertion with the contacts in the direction of the modiolus. Since the electrode wing is contralateral to the contacts, the surgical technique should be clear when using the wing for the insertion. This procedure and direction of contacts is clear for right ears when the right-handed surgeon holds the wing. Performing the same procedure in a left ear while holding the wing on the right side of the electrode as a right-handed surgeon led to an electrode contact direction away from the modiolus as shown in our experiments (Figures 2 and 4).

Our observations show that there is no significant effect of the contact position on neural response threshold in the slim straight electrode that was evaluated. This finding is in contrast to comparisons between lateral wall electrodes and perimodiolar electrodes and might be related to the relatively larger distance from the modiolus when comparing lateral wall electrodes with perimodiolar electrodes from the same producer[14,30]. The NRT levels for straight electrodes are higher than perimodiolar electrode arrays. This is the result of an improved electrode position along the lateral wall, lengthening the distance to the modiolus and spiral ganglion. If a scalar translocation accidentally occurs with a straight electrode, the distance between the electrode array and the spiral ganglion will be greater than in precontoured electrodes[10,22,31]. Therefore, the relative distance difference between lateral wall electrode contacts at different directions is smaller than for perimodiolar electrodes in cases of scalar translocation, or with or without a stylet [26,30.]

With slim straight electrodes, the direction of electrode contacts during cochlear implant electrode insertion in relation to the modiolus is assumed to be important for surgical handling and electrophysiological threshold.

Based on temporal bone in-vitro observations, electrode torsion does not occur during insertions with modiolus distant electrode contact direction.

Electrophysiological measurements evidence shows that intracochlear contact direction has no impact on neural response threshold in slim straight electrodes.

From this finding we can assume; 1. There is a ball-like current spread around each contact and not a cone-like current spread on the side of the electrode contacts. A cone-like current spread should have shown a higher neural response threshold for the lateral position, which is not the case. 2. Out of the missing neural response threshold difference between different contact positions, we can assume that a bilateral contact placement has no advantages (EVO electrode, MEDEL electrodes) in comparison to a unilateral placement.

Nevertheless, the number of the spiral cell ganglion should be kept in mind because even regional spiral ganglion cell degenerations are known to happen, and these parameters can also vary. So-called dead or semi-dead regions could cause threshold shifts with irregular neural response patterns. Furthermore, multiple scalar changes in the electrode array will influence the electrophysiologic parameters within the cochlea, and may influence the validity of the predictive value of the neural response threshold ratio[14].

A limitation in our study is the small sample size. Therefore, it is important to consider variables that may or may not exist between individuals. For example, the condition of the spiral ganglion and the depth of electrode insertion, as well as various pathologies that could cause deafness, influencing the symmetry of the neural response thresholds. The limited existing literature on this topic makes this study one the first of its kind to analyze this statement. Which opens the doors for future research. Hence, further investigation on this topic still is needed.

2.5. Conclusion

The contact direction of slim straight cochlear implant electrodes has no significant impact on NRT.

Our study shows that these results can be reproducible with slim straight electrodes. This is an important finding since when following the manufacturer's recommendations the contacts insertion in the direction to the modiolus it is not always possible. And it depends on the ear side to be operated on and the hand utilized by the surgeon (right- left). However, this technical difficulty can be overridden by holding the electrode wing. This facilitates the surgery since the insertion is carried out with greater insertion confidence. While understanding that similar outcomes can be achieved when the electrode is in either lateral or medial direction. Finally, this not increase the risk of surgery which provides the surgeon more confidence and security to achieve expected outcomes, regardless of the electrode position.

We presume that the contact electrode position should not have a future impact on hearing outcomes, such as speech understanding. We believe that this could be an important guide for surgeons who will be utilizing these electrodes in the future. The low intracochlear damage with better rest hearing preservation outcomes obtained with the slim straight electrode are also appealing. With no significant risk for intracochlear structures damage.

Clinical results are lacking, however this is a relatively new subject that has shown promising results. However, future work with long-term outcomes is necessary to prove efficacy and safety.

2.6. Disclosures

The electrode array used in this study was provided by the manufacturer (Cochlear Ltd.). There are no equity interest in the company, no royalties from products, no financial interest. Manufacture had the obligation to serve as the clinical research organization.

My job in this study was to drill the temporal bones as well as finding and analyzing the few published articles about the 522 slim straight electrode. I adjusted and prepared the microscope and AIDA documentation system to perform the insertions after preparation of the temporal bones. The electrode insertion require a lot of expertise, which is why this part was the only aspect of the study in which I did not take part. Because Ingo Todt is an experienced surgeon, he performed the insertions. While he was performing the insertions, my duty was to manage the microscope, focus the image and record the procedures. Finally, all the data were collected, analyzed and the results previously described were obtained. I also completed all the writing. Ingo Todt provided support of the discussion and certain corrections.

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3. Eidesstattliche Versicherung

„Ich, Juan Francisco Ordonez Cordova , versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: “Elektrophysiologische Effekte der slim straight intracochlearen
Elektrodenposition ”
“Effect of slim straight intracochlear electrode position on neural response thresholds” selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.
Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren beruhen, sind als solche in korrekter Zitierung kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) werden von mir verantwortet.

Ich versichere ferner, dass ich die in Zusammenarbeit mit anderen Personen generierten Daten, Datenauswertungen und Schlussfolgerungen korrekt gekennzeichnet und meinen eigenen Beitrag sowie die Beiträge anderer Personen korrekt kenntlich gemacht habe (siehe Anteilserklärung). Texte oder Textteile, die gemeinsam mit anderen erstellt oder verwendet wurden, habe ich korrekt kenntlich gemacht.

Meine Anteile an etwaigen Publikationen zu dieser Dissertation entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit dem/der Erstbetreuer/in,
angegeben sind. Für sämtliche im Rahmen der Dissertation entstandenen
Publikationen wurden die Richtlinien des ICMJE (International Committee of Medical Journal Editors; www.icmje.og) zur Autorenschaft eingehalten. Ich erkläre ferner, dass mir die Satzung der Charité – Universitätsmedizin Berlin zur Sicherung Guter Wissenschaftlicher Praxis bekannt ist und ich mich zur Einhaltung dieser Satzung verpflichte.

Weiterhin versichere ich, dass ich diese Dissertation weder in gleicher noch in ähnlicher Form bereits an einer anderen Fakultät eingereicht habe.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§§156, 161 des Strafgesetzbuches) sind mir bekannt und bewusst.

Datum Unterschrift

Anteilserklärung an den erfolgten Publikationen

Juan Francisco Ordonez Cordova hatte folgenden Anteil an folgender Publikation:

Publikation 1**: Ordonez F,** Sudhoff H, Todt I. Electrophysiological effects of slim straight intracochlear electrode position. The Journal of Laryngology and Otology, Vol.134 no.12, pp.1077-1080, 2020. Beitrag im Einzelnen:

Ich habe für diese Publikation alles selber berabeitet: Bohrungen der Felsenbeine, Messungen der Felsenbeine, Literaturrecherche, digitale und mikroskopische Erfassung der Elektrode Insertionen, Datensammlung, statistische Überprüfung und Auswertung. Ausarbeitung und Verfassung des Manuskripts.
Aus meiner statistischen Auswertung ist die Figur 3 entstanden. Figur 1 und 2 ergaben sich, die durch vom mir durchgeführte Bohrungen, Messungen sowie Digitale Erfassung. Anschließend habe ich ebenfalls selber alles mit der entsprechende Literatur zusammen gefasst und darauf resultierte die o.g. Publikation.

Das Einsetzen der Elektroden erfordert viel Erfahrung und Fachwissen und als Assistenzarzt, darf man noch nicht selbständig mit den Implantaten umgehen, weshalb war dieser Teil der einzige Aspekt der Studie, an dem ich nicht teilgenommen habe. Da Ingo Todt (Erste Betreuer) ein erfahrener Chirurg ist, führte er die Insertionen durch.

Unterschrift, Datum und Stempel des/der erstbetreuenden Hochschullehrers/in

Unterschrift des Doktoranden/der Doktorandin

4. Auszug aus der Journal Summary List

Journal Data Filtered By: **Selected JCR Year: 2018** Selected Editions: SCIE,SSCI Selected Categories: **“OTORHINOLARYNGOLOGY”** Selected Category Scheme: WoS

Gesamtanzahl: 42 Journale

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
1	JAMA Otolaryngology-Head & Neck Surgery	2,855	3.502	0.012700
2	RHINOLOGY	2,602	3.354	0.002200
3	DYSPHAGIA	3,367	3.034	0.003470
4	EAR AND HEARING	5,747	2.954	0.006800
5	HEARING RESEARCH	9,237	2.952	0.010490
6	JOURNAL OF VESTIBULAR RESEARCH-EQUILIBRIUM & ORIENTATION	1,117	2.774	0.001440
7	Trends in Hearing	442	2.768	0.001710
8	JARO-JOURNAL OF THE ASSOCIATION FOR RESEARCH IN OTOLARYNGOLOGY	2,145	2.716	0.003400
9	International Forum of Allergy & Rhinology	2,380	2.521	0.006570
10	HEAD AND NECK-JOURNAL FOR THE SCIENCES AND SPECIALTIES OF THE HEAD AND NECK	11,100	2.442	0.018120
11	CLINICAL OTOLARYNGOLOGY	3,412	2.377	0.003940
12	LARYNGOSCOPE	22,642	2.343	0.026200
13	OTOLARYNGOLOGY-HEAD AND NECK SURGERY	13,643	2.310	0.017500
14	Journal of Otolaryngology-Head & Neck Surgery	1,910	2.175	0.002330
15	OTOLOGY & NEUROTOLOGY	8,094	2.063	0.011170
16	AUDIOLOGY AND NEURO-OTOLOGY	1,825	2.053	0.002500
17	American Journal of Rhinology & Allergy	3,290	2.015	0.004050
18	INTERNATIONAL JOURNAL OF AUDIOLOGY	3,598	1.821	0.004600
19	EUROPEAN ARCHIVES OF OTO-RHINO-LARYNGOLOGY	8,038	1.750	0.015250

1

Selected JCR Year: 2018; Selected Categories: “OTORHINOLARYNGOLOGY”

Rank	Full Journal Title	Total Cites	Journal Impact Factor	Eigenfactor Score
20	OTOLARYNGOLOGIC CLINICS OF NORTH AMERICA	2,643	1.620	0.002650
21	Brazilian Journal of Otorhinolaryngology	1,481	1.603	0.002250
22	Clinical and Experimental Otorhinolaryngology	655	1.550	0.001440
23	ANNALS OF OTOLOGY RHINOLOGY AND LARYNGOLOGY	6,428	1.458	0.004320
24	JOURNAL OF VOICE	4,534	1.453	0.004260
25	AURIS NASUS LARYNX	2,087	1.444	0.002870
26	Acta Otorhinolaryngologica Italica	1,486	1.408	0.001980
27	ENT-EAR NOSE & THROAT JOURNAL	1,641	1.375	0.001000
28	Journal of the American Academy of Audiology	2,238	1.358	0.002250
29	American Journal of Audiology	817	1.340	0.001580
30	European Annals of Otorhinolaryngology-Head and Neck Diseases	760	1.318	0.001470
31	Current Opinion in Otolaryngology & Head and Neck Surgery	1,861	1.293	0.002390
32	ACTA OTO-LARYNGOLOGICA	6,608	1.286	0.004890
33	JOURNAL OF LARYNGOLOGY AND OTOLOGY	5,439	1.261	0.004370
34	INTERNATIONAL JOURNAL OF PEDIATRIC OTORHINOLARYNGOLOGY	7,275	1.225	0.009960
35	ORL-Journal for Oto-Rhino-Laryngology Head and Neck Surgery	309	1.052	0.000890
36	AMERICAN JOURNAL OF OTOLARYNGOLOGY	2,668	0.932	0.003240
37	HNO	1,154	0.914	0.001110
38	LARYNGO-RHINO-OTOLOGIE	880	0.853	0.000520
39	Logopedics Phoniatrics Vocology	413	0.818	0.000480
40	Journal of International Advanced Otology	284	0.735	0.000760
41	FOLIA PHONIATRICA ET LOGOPAEDICA	945	0.544	0.000630

Selected JCR Year: 2018; Selected Categories: “OTORHINOLARYNGOLOGY”

42	B-ENT	421	0.263	0.000550

5. Druckexemplar der ausgewählten Publikation

- Ordonez F**,** Sudhoff H, Todt I. Electrophysiological effects of slim straight intracochlear electrode position. The Journal of Laryngology and Otology, Vol.134 no.12, pp.1077-1080, 2020.

- DOI: https://doi.org/10.1017/S0022215120002534

- Ordonez F**,** Sudhoff H, Todt I. Electrophysiological effects of slim straight intracochlear electrode position. The Journal of Laryngology and Otology, Vol.134 no.12, pp.1077-1080, 2020.

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- DOI: https://doi.org/10.1017/S0022215120002534

6. Lebenslauf

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

7. Publikationsliste

- **Ordonez F,** Sudhoff H, Todt I. Electrophysiological effects of slim straight intracochlear electrode position. The Journal of Laryngology and Otology, Vol.134 no.12, pp.1077-1080, 2020.

- Ordonez F, Riemann C, Mueller S, Sudhoff H, Todt I. Dynamic intracochlear pressure measurement during cochlear implant electrode insertion. Acta Oto-Laryngologica, Vol. 139, no. 10, pp. 860-865, 2019.

Kongressvorträge/posters

- 89. Jahresversammlung der deutschen Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie e.V., Lübeck, 09.-12.05.2018: Intraoperative Korrelation zwischen NRT Schwelle und Elektrodeninsertion
  mit der Cochlear slim straight Elektrode (Poster). Ordonez F, Scholtz LU, Müller S, Tek F, Seitz D, Sudhoff H und Todt I..

8. Danksagung

Ich möchte mich bei Herrn Prof. Dr. med. Holger Sudhoff, dem Klinikdirektor der Klinik für Hals-Nasen-Ohrenheilkunde, Kopf- und Hals-Chirurgie des Klinikums Bielefeld Mitte bedanken, da ich die Möglichkeit hatte, an seiner Klinik und an seinem Felsenbeinlabor ein Teil unserer Studie durchzuführen.

Ebenso werde ich an meinem Doktorvater Herrn PD Dr. med. Ingo Todt immer dankbar sein. Er hat mich gefördert mit dieser Arbeit zu beginnen. Außerdem bedanke ich mich bei ihm für seine kontinuierliche Unterschtützung. Die Leidenschaft, das Engagement und die Kreativität, mit denen er jede Studie durchführt, haben mich motiviert mein Ziel zu erreichen.

Mein Erfolg gehört auch meiner Familie, deshalb möchte ich mich zuletzt bei meiner Frau Emilia Quintanilla, meinen Kinder und meinen Eltern bedanken. Ohne ihre Geduld sowie ständige Unterstützung, wäre es nicht möglich gewesen. Dafür werde ich lebenslang dankbar sein.