Research paper

Insertion site and sealing technique affect residual hearing and tissue formation after cochlear implantation

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ABSTRACT

Tissue formation around the electrode array of a cochlear implant has been suggested to influence preservation of residual hearing as well as electrical hearing performance of implanted subjects. Further, inhomogeneity in the electrical properties of the scala tympani shape the electrical field and affect current spread. Intracochlear trauma due to electrode insertion and the insertion site itself are commonly seen as triggers for the tissue formation. The present study investigates whether the insertion site, round window membrane (RWM) vs. cochleostomy (CS), or the sealing material, no seal vs. muscle graft vs. carboxylate cement, have an influence on the amount of fibrous tissue and/or new bone formation after CI implantation in the guinea pig. Hearing thresholds were determined by auditory brainstem response (ABR) measurements prior to implantation and after 28 days. The amount of tissue formation was quantified by evaluation of microscopic images obtained by a grinding/polishing procedure to keep the CI in place during histological processing.

An insertion via the round window membrane resulted after 28 days in less tissue formation in the no seal and muscle seal condition compared to the cochleostomy approach. Between these two sealing techniques there was no difference. Sealing the cochlea with carboxylate cement resulted always in a strong new bone formation and almost total loss of residual hearing. The amount of tissue formation and the hearing loss correlated at 1–8 kHz. Furthermore, the use of carboxylate cement as a sealing material in cochlear implantation should be avoided even in animal studies, whereas sealing the insertion site with a muscle graft did not induce an additional tissue growth compared to omitting a seal. For hearing preservation the round window approach should be used.

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1. Introduction

Subjects with severe to profound hearing loss can benefit from a cochlear implant (CI). Even though this is the method of choice, some challenges still remain with this treatment, especially with regard to preservation of residual hearing for electro-acoustic stimulation (EAS).

After implantation a fibrous tissue sheath or, in some cases, new bone develops around the electrode carrier, particularly in the basal turn (Li et al., 2007). Impedances also increase after implantation (Busby et al., 2002). As shown in cats (Clark et al., 1995), these impedances correlate with the amount of fibrous tissue found around the CI electrode. Additionally, the formation of tissue seems to start at the cochleostomy, as the impedance increases are fastest and largest at the basal electrodes (Paasche et al., 2006). Furthermore, Kawano et al. (1998) report a correlation between the amount of fibrous tissue and/or new bone formation and the hearing performance of the individuals, probably due to an increased distance between electrodes and Rosenthal’s canal and an altered current spread. Not only electrical stimulation is influenced by the formation of fibrous and bony tissue, also the residual hearing may be influenced by it (Choi and Oghalai, 2005; O’Leary et al., 2013). Generally, the post-operative tissue formation is considered to be a component of the late cochlear damage and a contributor to the host response following CI implantation (Li et al., 2007; Somdas et al., 2007).

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Provided that the source of the tissue formation is the insertion site, this site and the sealing thereof may determine the amount of fibrous tissue after CI implantation. Currently, there are two main insertion sites used for cochlear implantation: An incision of the round window membrane (RWM) or a cochleostomy (CS), usually in the basal turn of the cochlea. The insertion via a cochleostomy allows a straight insertion of the implant and is thus often considered the standard implantation site. However, it involves drilling of an opening in the bony wall of the cochlea, which can lead to noise exposure up to 130 dB sound pressure level (SPL) (Pau et al., 2007) and risks the entry of bone particles into the cochlea. Additionally, it may damage the stria vascularis or cochlear vessels. The round window approach leads to less insertion trauma in the basal turn of the cochlea (Richard et al., 2012) and is therefore recommended if hearing preservation is desired after implantation (Lenarz et al., 2006).

Several different sealing techniques are used in human or animal studies to seal the insertion site; including no seal (Purser et al., 1991; Kral et al., 2002) as well as an autologous muscle or fascia graft (Friedland and Runge-Samuelson, 2009) and the use of carboxylate cement (Scheper et al., 2009). The aim of the current study was to investigate the influence of the different insertion and sealing techniques on the formation of fibrous tissue and/or new bone and on the hearing performance after CI model implantation in normal hearing guinea pigs.

2. Materials and methods

All experiments had been approved by the Institutional Animal Care and Research Advisory Committee and the local ethics committee. The study has been conducted in accordance with the German “Law on Protecting Animals” and with the European Communities Council Directive 86/609/EEC for the protection of animals used for experimental purposes.

2.1. Electrode model

A platinum (Pt) wire with a diameter of 0.19 mm was dip-coated with medical grade silicone (NuSil Med 4234; NuSil Technology LLC, Carpintiera, USA). The diameter of the CI implant model was kept between 0.4 and 0.6 mm with a length of 7 mm. Additionally 4 electrode models with the same diameter and length as the other CI models but without Pt wires were manufactured in a mold. Prior to implantation the CI models were sterilized in an autoclave to allow aseptic insertion.

2.2. Study design

In this study 60 normal hearing Dunkin Hartley guinea pigs (Charles River Laboratories International Inc., Sulzfeld, Germany) were implanted unilaterally with a CI electrode model. Half of the animals were implanted via the round window membrane (RWM), the other half via a cochleostomy. After implantation the insertion site was either left open (no seal, NS) or sealed with a muscle tissue graft (muscle seal, MS) or carboxylate cement (Durelon™, 3M ESPE AG, Seefeld, Germany) (Durelon™ seal, DS). Thus 6 groups combining each insertion site with each sealing technique were implanted. The hearing thresholds of the animals were determined on day 0 prior to surgery and on day 28.

2.3. Anesthesia

Implantations and measurements were performed under general anesthesia. The animals were anesthetized with an intramuscular (i.m.) injection of a combination of 0.025 mg/kg fentanyl citrate (Janssen-Cilag GmbH, Neuss, Germany), 0.2 mg/kg medetomidine hydrochloride (Janssen-Cilag GmbH) and 1 mg/kg midazolam (Ratiopharm GmbH, Ulm, Germany). Pretreatment was done with 0.05 mg/kg atropine sulfate (B. Braun Melsungen AG, Melsungen, Germany) applied subcutaneously (s.c.). The animals received supplementary doses of anesthetics i.m. to maintain anesthesia if needed.

The animals were supplemented s.c. with 26 mL/kg Ringer acetate and glucose 5% (ratio 1:1) at the beginning of the anesthesia as well as after finishing the surgery. For analgesia the animals received 5 mg/kg carprofen (Pfizer GmbH, Berlin, Germany) s.c. Additionally, animals received 10 mg/kg enrofloxacin (Bayer AG, Leverkusen, Germany) s.c. as antibiotic treatment during surgery as well as the 5 following days per os (p.o.).

After surgery on day 0 the anesthesia was reversed with an i.m. injection of a combination of 1 mg/kg naloxone hydrochloride (Intresa Arzneimittel GmbH, Freiburg, Germany), 0.1 mg/kg flumazenil (Intresa Arzneimittel GmbH) and 0.03 mg/kg atipamezole hydrochloride (Janssen-Cilag GmbH).

To prevent any disturbances of the gastro-intestinal tract the animals were fed 0.5 g BeneBac® Gel (Albrecht GmbH, Aulendorf, Germany) p.o. one day prior to surgery, the day of surgery and the following day.

During all experiments the animals were kept on a heating pad to avoid hypothermia.

2.4. ABR measurements

To determine the hearing threshold of the animals prior to surgery, and to detect any threshold shift during the experiment, acoustically evoked auditory brainstem response (aABR) measurements were performed under general anesthesia at the beginning of the experiment (day 0) as well as at the end (day 28).

In a sound-attenuated chamber the animals were presented frequency specific acoustic tone stimuli (10 ms tone bursts with a square cosine rise and fall time of 1 ms) with a loudspeaker connected via a calibrated tube to the outer ear canal. The animals were stimulated with a TDT System (Tucker–Davis Technologies, Alachua, USA) at frequencies of 1, 4, 8, 16, 32, 40 kHz from 0 to 90 dB in 10 dB steps. Each stimulus was presented 85 times per set and 3 sets were obtained.

Subdermal needle electrodes (CareFusion Nicolet, CareFusion Corporation, San Diego, USA) were placed on the left and right mastoid (references), in the neck (ground) and at the vertex (common positive).

Acquisition and analysis were performed with BioSigRP software (Tucker–Davis Technologies). Obtained signals were amplified (20 times), bandpass filtered (300–3000 Hz) and every set of 85 signals was averaged. All 3 sets were averaged together and the lowest intensity which evoked a visually replicable waveform with decrements of peak latencies with increasing sound pressure level was defined as the hearing threshold.

2.5. Surgery

Following the ABR measurements the animals underwent surgery under aseptic conditions. After a postauricular incision the muscle was dissected until the bulla was in plain view. The bulla was opened with a scalpel. Then the cochlea and the round window membrane (RW) were visualized and either the latter was incised with a knife or a hole was drilled into the cochlear ventral of the RW with a 0.6 mm diamond burr (cochleostomy, CS).

After insertion of the CI model the insertion site was either left “open” (NS), sealed with a small autologous muscle graft (MS) or the gap between CI model and the opening of the cochlea was sealed, DS). Thus 6 groups combining each insertion site with each sealing technique were implanted. The hearing thresholds of the animals were determined on day 0 prior to surgery and on day 28.
closed with Durelon<sup>™</sup> (DS). Each sealing technique was combined with both insertion sites. After implantation the bulla defect was closed with Durelon<sup>™</sup>, muscle and skin were sutured. The contralateral side remained unimplanted and served as a control for the ABR measurements.

2.6 Preparation and histology of the cochleae

After being implanted for 28 days the animals were euthanized under deep anesthesia via transcardial perfusion of phosphate buffered saline followed by modified Wittmaak’s fixation solution. The cochleae were harvested and after opening of the apex postfixed for 18 h in modified Wittmaak’s fixation solution. After a washing step in Li<sub>2</sub>SO<sub>4</sub> for 18 h, the cochleae were dehydrated in ethanol (50%, 70%, 90% and 100%), washed with TEK M E K<sup>®</sup> (Struers GmbH, Willich, Germany) and embedded in epoxy (Spezifix 40<sup>®</sup>, Struers). The embedded cochleae were ground with a grinder/polisher (PowerPro<sup>™</sup> 4000, Buehler GmbH, Düsseldorf, Germany) set to 40 μm grinding steps. The polished surface was stained with Kallicichrom (Waldeck GmbH & Co. KG, Münster, Germany) for 90 s, rinsed and photographed using a VHX 600 microscope system (Keyence Deutschland GmbH, Neu-Isenburg, Germany) at magnifications of 30×, 50×, 100× and 200×. In every second “section” of the ground cochlea the area of fibrous tissue and new bone formation was measured with the VHX 600 software (Keyence). For this purpose the area covered by fibrous or bony tissue was determined by tracing its borders. The areas for each tissue were summed up. To determine the absolute volume of newly-formed tissue, this area was multiplied by the intersection distance (80 μm). These values (μm³) were converted to microliter.

2.7 Data analysis

Only animals with an initial ABR hearing threshold below 50 dB SPL at the point of the best hearing (8–16 kHz) and no severe mechanical trauma during implantation (e.g. damage to the modiolus) were included in this study. Exclusion criteria were a survival time of less than 28 days and signs of middle or inner ear infection in histology.

All statistical analysis was performed with SPSS (IBM Deutschland GmbH, Ehningen, Germany) or Prism software (GraphPad Software, Inc., La Jolla, USA). If not stated otherwise the graphs were plotted as mean ± standard deviation (SD) using Prism software (GraphPad Software, Inc.). For statistical analysis of the hearing thresholds all thresholds on day 28 above stimulation level (90 dB SPL) were defined as 100 dB SPL to allow calculating the threshold shift. Animals with no detectable hearing threshold at specific frequencies on day 0 were not included in statistical evaluation at this frequency. An overview on animals without detectable hearing thresholds on day 0 is given in Table 1 and on day 28 in Table 2.

As the number of animals per group was five, non-parametric tests were performed. A Kruskal–Wallis Test was performed for group comparison. If this test showed a significant difference between groups with an error probability α < 0.05, then two-tailed Mann-Whitney-U tests were performed between individual groups. Assessment of a correlation between tissue formation and hearing threshold was performed with a Spearman–Rho-test. In all tests differences with α < 0.05 were considered as significant.

3 Results

Due to several reasons 30 animals had to be excluded from this study (survival time of less than 28 days: n = 3, signs of middle ear infection: n = 2, damage of the cochlea during histological preparation: n = 1, mechanical trauma: n = 24). One animal had the frequency with lowest thresholds at 16 kHz (30 dB SPL) and was included into the study even though the threshold at 8 kHz was 90 dB SPL.

3.1 ABR measurements

The average hearing thresholds before implantation for all included animals and ears as well as the hearing thresholds 28 days after implantation for the implanted ears and the control ears are illustrated in Fig. 1. After 28 days, control ears showed a small but significant threshold shift of 5–8 dB SPL only at 4 and 8 kHz compared to the average threshold of all animals on day 0. In contrast, thresholds were increased (P < 0.001) in implanted ears

Table 2

<table>
<thead>
<tr>
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<th>Sealing technique</th>
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<th>8 kHz</th>
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Fig. 1. Average hearing threshold before and after implantation. Hearing threshold (mean ± SD) before implantation on day 0 (black crosses) for all ears and on day 28 for implanted (dark gray squares) and control ears (light gray circles). The upper asterisks represent differences between implanted ears and both other groups (**P < 0.001) and the lower asterisks indicate a difference between control group on day 28 and all ears on day 0 (**P < 0.05).
at all frequencies compared to thresholds on day 0 and to control ears on day 28.

At 4 kHz, the MS group in the RWM approach showed lower hearing thresholds (72 ± 4.9 dB SPL) than all other groups (RWM NS: 97 ± 2.5 dB SPL, P = 0.024; RWM DS: 100 ± 0 dB SPL; CS NS: 94 ± 6 dB SPL, P = 0.041; CS MS: 94 ± 6 dB SPL, P = 0.041; CS DS: 98 ± 2 dB SPL, P = 0.015). Similar results were observed at 1 kHz even though not statistically evaluated. In some animals the threshold could not be determined at some frequencies. The number of animals without detectable thresholds was generally larger at 32 and 40 kHz compared to the lower frequencies (Table 2).

The pooled CS insertion groups (n = 15) had higher hearing thresholds than the RWM groups when compared at 8 kHz on day 28 (n = 15; P = 0.042). Comparing the different sealing techniques, the DS group had a tendency to higher thresholds, but this difference was not significant. At all other frequencies, hearing was completely lost in both DS conditions with the exception of one animal of the CS DS group that had a high threshold of 90 dB SPL at 1 and 4 kHz (Table 2).

Regarding the threshold shift at 8 kHz (Fig. 2), there was no difference between the RWM groups and the CS groups (P = 0.34). The comparison of the different sealing techniques, regardless of the insertion site, revealed significant differences (Kruskal–Wallis test: P = 0.016). The DS group had larger threshold shifts (n = 10, 65 ± 2.7 dB) than the other sealing techniques used (NS (n = 10): 41 ± 8.1 dB, P = 0.007; MS (n = 10): 50 ± 6.3 dB, P = 0.049). At 4 kHz, no differences between the insertion sites were found (RWM: n = 14, 37.1 ± 5 dB; CS: n = 15, 38.7 ± 4.2 dB; P = 0.947). Also the different sealing techniques did not lead to significant differences (Kruskal–Wallis test: P = 0.064; NS: n = 9, 41.1 ± 6.1; MS: n = 10, 28 ± 5.1; DS: n = 10, 45 ± 4.3 dB). Similar results were found at 1 kHz for the insertion site comparison (RWM: n = 13, 20 ± 4.5 dB; CS: n = 9, 20 ± 3.3 dB) as well as for the sealing techniques used (NS: n = 7, 18.6 ± 4 dB; MS: n = 8, 8.8 ± 3.5 dB; DS: n = 7, 34.3 ± 2 dB).

3.2. Histology

An example of the position of the CI model in the cochlea is shown in the midmodiolar overview of an implanted cochlea in Fig. 3A as well as on the 3D-reconstruction in Fig. 3B. After 28 days implantation time the insertion site was closed in all conditions (Fig. 3C). At the cochleostomy site the newly formed bone often reached into the scala tympani (ST) (Fig. 3C). This bone formation was found both apical and basal of the cochleostomy site. Additionally, on each CI model’s surface there was a thin layer of fibrous tissue. In every single cochlea with a Durelon™ sealing, regardless
whether implanted via the round window or a cochleostomy, there was profound new bone formation in the basal turn (Fig. 3D). This was not the case in the cochleae of the other groups.

Significantly more tissue (fibrous tissue + bone formation) was found in the CS condition than in the RWM condition if no seal \( (P = 0.032) \) or a muscle seal \( (P = 0.008) \) was used. In the bone cement groups there was no difference between the two insertion sites.

With the RWM approach (Kruskal–Wallis test: \( P = 0.009 \)) a larger volume of new tissue was detected in the DS group (0.73 ± 0.15 \( \mu \)L) compared to the two other sealing techniques (NS: 0.028 ± 0.01 \( \mu \)L, \( P = 0.008 \); MS: 0.025 ± 0.01 \( \mu \)L, \( P = 0.008 \)) (Fig. 4). There was no difference between these two latter groups. In the CS groups the volumes were different (Kruskal–Wallis test: \( P = 0.035 \)) and the largest volume of new tissue formation was also found in the DurelonTM group (0.59 ± 0.23 \( \mu \)L). This volume was significantly larger in comparison to the NS condition (0.12 ± 0.05 \( \mu \)L, \( P = 0.032 \)) but not in comparison to the MS condition (0.23 ± 0.11 \( \mu \)L, \( P = 0.056 \)).

With the RWM approach (Kruskal–Wallis test: \( P = 0.0075 \)) more fibrous tissue was formed with the Durelon seal (0.289 ± 0.13) than with the other sealing techniques (NS: 0.027 ± 0.013, \( P = 0.0079 \); MS: 0.0148 ± 0.006, \( P = 0.0079 \)). There were no differences in the amount of fibrous tissue when using the cochleostomy approach. Additionally, there was no difference between the two insertion sites for each sealing technique.

Almost no new bone formation was detected in the RWM condition with the use of no seal or muscle seal (NS: 0.001 ± 0.001 \( \mu \)L; MS: 0.01 ± 0.01 \( \mu \)L). In the CS approach there was only a small amount of new bone formation with these sealing techniques (0.1 ± 0.04 \( \mu \)L, 0.2 ± 0.09 \( \mu \)L, respectively). In both DS groups (RWM and CS) a large volume of new bone was found (CS: 0.51 ± 0.21 \( \mu \)L, RWM: 0.44 ± 0.14 \( \mu \)L).

### 3.3. Correlation between ABR and histology

In Fig. 5 the threshold shift at 8 kHz is plotted in relationship to the tissue formation. In animals with a tissue formation of less than 0.1 \( \mu \)L the threshold shift was between –10 dB SPL and 70 dB SPL. All animals with a tissue formation of more than 0.7 \( \mu \)L had threshold shifts of 70 dB SPL or more. The figure also shows that a hearing loss of ≤50 dB SPL was only observed in animals with less than 0.3 \( \mu \)L tissue formation. There is a correlation between the amount of new tissue formation and the detected threshold shift at the frequencies from 1 to 8 kHz (Table 3), which is mostly due to the correlation between new bone formation and hearing threshold as there was only a correlation between fibrous tissue formation and threshold shift at 1 kHz (\( r = 0.703, P = 0.0003 \)).

### 4. Discussion

The present study demonstrates for the first time that different cochlear approaches and sealing techniques significantly affect tissue growth and residual hearing after cochlear implantation. It demonstrates that cochleostomy as well as the use of a carboxylate cement to seal the cochlea both induce enhanced fibrous tissue and bone growth. Finally, these approaches are also associated with a more severe loss of hearing.

The design of this study was focused on the determination of the influence of the sealing technique and insertion site on tissue formation, but not on hearing preservation. The disadvantage of this approach was the relatively large hearing threshold shift in all groups. Nevertheless differences between groups were still detectable.

Traditionally, the investigation of tissue growth is limited to midmodiolar sections or only few slice positions along the cochlea (O’Leary et al., 2013; Farhadi et al., 2013). Consequently, the results do not reflect the full extent of tissue growth in the whole inner ear. To circumvent this problem, and to exclude the possibility of a (partial) removal of intracochlear tissue with the retraction of the electrode model, a grinding technique has been used in the present study. A section distance of 80 \( \mu \)m allowed the reconstruction of the tissue formation in the cochlea.

The grinding technique is a suitable method for histological preparation of the cochlea with an implanted stimulation electrode (Stöver et al., 2005), as it allows avoiding technical problems with...
two approaches (Adunka et al., 2006), but the authors speculate that these different findings may be due to different electrode designs in the different studies.

The current study further demonstrated a greater fibrous tissue and bone formation in the cochleostomy groups compared to the RWM groups. This tissue formation was always located near the cochleostomy. Consequently, the trauma of a cochleostomy itself appears greater than the trauma of an incision of the round window membrane. The slightly larger hearing loss in the CS groups might be due to this tissue formation or due to the noise trauma inflicted with the drilling procedure (Pau et al., 2007). Another possible reason is an entry of bone dust into the cochlea. A bone paté sealing can indeed result in a drop of hearing performance in CI users and even in a repulsion of the implant due to an extensive new bone formation (McElveen et al., 1995).

The seal used for CI implantation is most commonly an autologous fascia or muscle graft although the use of different materials such as fat (Nadol and Eddington, 2004), bone paté (McElveen et al., 1995) or no seal (Purser et al., 1991) was also reported. The seal plays an important role as it ensures the sealing of the inner ear towards the middle ear and thus re-establishes the separation of liquor and middle ear environment. A sufficient seal is of major importance for the prevention of progression of middle ear infections into the inner ear and the brain. If no seal is used, the gap between implant and RWM is still not closed completely up to 5 months post implantation (Franz et al., 1984). Although the seal helps to re-establish the barrier between inner ear and middle ear faster, it also holds the potential of being the origin of tissue growth into the cochlea.

To investigate whether the use of a seal has an influence on tissue formation and/or hearing threshold, two groups did not receive any seal, the other groups received a seal which consisted either of a muscle graft or an abiotic seal of Durelon™. The latter material has been commonly used in animal studies to close the bulla defect and in some studies also the cochlear opening (Schepker et al., 2009; Warnecke et al., 2012).

As there was almost no difference between the no seal and muscle seal groups – neither with regard to hearing thresholds nor with regard to the amount of tissue formation as found 28 days after implantation – there seems to be no disadvantage in using an autologous muscle graft to seal the insertion site. It is recommendable to establish an effective barrier as soon as possible after implantation. The use of carboxylate cement as a sealing material in CI implantation leads to a very strong new bone formation and should be avoided also in animal research. In all animals using the cement, regardless whether implanted via the RWM or a CS, most of the basal turn was filled with new bone. This might also explain the larger threshold shift observed in these groups, as the amount of tissue growth in the basal turn of the cochlea has an impact on the hearing thresholds (O’Leary et al., 2013). In the current study a statistical evaluation of a possible correlation between tissue formation and threshold shift at the basally located frequencies was omitted as the hearing thresholds at these frequencies were above the detectable level in most of the animals, possibly due to the location of the initial insult in this area. The study revealed a correlation between the amount of tissue formation and hearing loss at frequencies of 1–8 kHz, which are frequencies represented more apical than the observed tissue formation. According to the relationship between distance from the basal end of the cochlea and the characteristic frequency (CF) as given by Robertson (1984) we expect that the tip of our CI model should be located at a CF of 12–16 kHz. Therefore all tested frequencies below 16 kHz should not directly be affected by cochlear implantation. However, some studies claim that dampening of the basilar membrane (BM) movement in the basal part of the cochlea may increase hearing...
thresholds in the apical frequency regions (Choi and Ogahalai, 2005).

A more plausible explanation is that the amount of tissue formation is an indicator for the strength of inflammation, which can influence not only the tissue formation but also the survival of hair cells (O’Leary et al., 2013). Unfortunately, hair cells and spiral ganglion neurons could not be investigated in the present histological method that is strongly focused on a detailed evaluation of the tissue growth in the entire cochlea. Therefore we cannot exclude that damage and/or loss of hair cells and/or spiral ganglion neurons also contributed to the elevation in hearing threshold. Even though the mechanisms are not completely clear, yet, our results demonstrate that the sealing techniques can affect the hearing thresholds at positions apical to the implanted cochlear partition.

5. Conclusion

The results of this study show that tissue formation in the basal turn of the cochlea cannot only influence the hearing performance of CI users (Kawano et al., 1998) or the impedance increase at the electrode contacts (Busby et al., 2002), but can also have an impact on the residual hearing at lower frequencies, which confirms the results of O’Leary et al. (2013). The use of carboxylate cement as a sealing material should be avoided even in animal experiments. The findings of this study support the implantation through the RWM. Furthermore, the fact that the sealing has an influence on the formation of fibrous tissue or new bone supports the assumption that the tissue growth starts at the insertion site and progresses from this point on further along the electrode array.

Conflict of interest

The authors declare that they have no conflict of interest.

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