The Version of Record of this manuscript has been published by Elsevier in Hearing Research on 15 September 2020, available at

<https://doi.org/10.1016/j.heares.2020.108018>

Please cite as: D'hondt C, Wouters J, Verhaert N. In-situ sensitivity of a totally-implantable microphone. Hear Res. 2020 Sep 15;395:108018. doi: 10.1016/j.heares.2020.108018. Epub 2020 Jul 8. PMID: 32712510.

1 Introduction

Fully-implantable active middle ear implants (AMEI)¹ have been commercially available for several years and are recognized as a treatment option for a variety of audiological and medical indications (Bruschini et al., 2009; Martin et al., 2009; Siegert et al., 2007). In addition to audiological and medical criteria, candidate selection should also include psychological, socioeconomical and clinical assessments (Wagner et al., 2010). Currently, there are two fully-implantable AMEIs on the market. The first one is the Esteem[®] system from Envoy Medical (Envoy Medical Corporation, White Bear Lake, Minnesota, USA). It is indicated for moderate to severe sensorineural hearing loss and its clinical results were published by several authors (Kraus et al., 2011; Maurer and Savvas, 2010; Pulcherio et al., 2014). The second one is the Carina[®] system from Cochlear[™] (Cochlear Ltd., Sydney, Australia). It is indicated for moderate to severe sensorineural or mixed hearing loss. Several publications have reported on the clinical results with the Carina system and show that it is safe and effective (Bruschini et al., 2016; Peixoto et al., 2019; Savaş et al., 2016; Uhler et al., 2016). Lefebvre et al. (2017) focused on the microphone of the Carina system and reported on the most prevalent microphone location and the correlation of the location with system feedback (whistling). The first available fully-implantable AMEI on the market was the totally implantable communication assistance TICA (Zenner and Rodriguez Jorge, 2010). The TICA system was indicated for sensorineural hearing loss. However, it was only clinically available until 2000.

One of the key components of fully-implantable hearing devices is the implantable microphone. Over the past years, important research advances have been made in the development of totally-implantable microphones (TIM). TIMs must fulfil several requirements. Firstly, they must fulfil technical requirements like e.g. sensitivity, dynamic range and bandwidth to be able to pick up speech sounds inside the human body. Secondly, they must comply with specific requirements for implantable devices: they must be biocompatible, small in size, hermetically sealed and designed such that they can stay and function in the human body for several years. At the same time TIMs should not be sensitive to body sounds induced by e.g. blood flow or chewing. Three TIM technologies have made their way into a commercial device. The Esteem system makes use of a piezoelectric force sensor that picks up sound vibrations from the ossicular chain. The Carina system comprises a subcutaneous electret condenser microphone that is implanted in the bone behind the ear, and the TICA used a subcutaneous microphone, which was implanted in the posterior auditory canal wall close to the eardrum. There are also several other developments in the field of implantable microphones. A technical review and evaluation of various implantable sensors for hearing devices is given by Calero et al. (2018).

A crucial parameter when characterizing microphones is the acoustic sensitivity. The sensitivity of a microphone is defined as the ratio of the output voltage to the input sound pressure. For an analog microphone, sensitivity, in units of mV/Pa, can be expressed logarithmically in dB V. For TIM, also the sensitivity to body sounds, i.e. vibrations, is important. However, the focus of this work is on the acoustic sensitivity of TIM. Research questions dealing with the TIM sensitivity to body sounds are out of scope and not covered in this work.

The acoustic sensitivity of TIMs can be tested on the bench. No measurement standard is existing for that, probably because the microphone technologies and applications are very different between the available TIMs. Admittedly, for a subcutaneous microphone it is challenging to simulate the skin. Not

¹ AMEI: Active middle ear implant; TIM: Totally implantable microphone; BAP: button audio processor

only does a good skin mimicking material² has to be found, also the variability in skin thickness, skin tension, etc. should be taken into account. The skin thickness is influenced by gender and age (Firooz et al., 2017) and is 6 mm on average in the mastoid region (Mylanus et al., 1994). While the average skin thickness is used for bench measurements, the variability of it can be simulated in models.

Once the TIM is implanted, its overall performance changes and is defined by both its technical performance characteristics and the individual skin and soft tissue characteristics of the implanted subject's anatomical coupling site. Directly after surgery, the formation of scar tissue or the presence of air on top of the microphone membrane might also influence the TIM sensitivity. The pre-operative (pre-op) measurements are a good way to characterize the TIM. However, the post-operative (in-situ) processes and tissue characteristics will cause a change in the microphone performance and will therefore influence the system performance and possibly the patient's speech performance.

The activation of the fully-implantable AMEI used in our study normally takes place 6-8 weeks after surgery to allow for healing. However, no data is available on how the healing process influences the system performance over time and the optimal waiting period before activation of the fully-implantable AMEI. Relevant research was done on the output/actuator site and on the feedback path (Banakis Hartl et al., 2017; Gamm et al., 2019; Grossöhminen et al., 2017), but limited data is available on the input/microphone side. It is important to know the TIM sensitivity in the body (in-situ sensitivity) as it is used as an input parameter for the fitting algorithm and influences the achievable gain. Therefore, this study aimed at answering the following two research questions:

1. How does the TIM acoustic sensitivity change once the TIM is implanted (pre-op vs. in-situ)?
2. How does the TIM acoustic sensitivity change over time from implantation to activation (short-term) and beyond (mid-term)?

2 Material & Methods

The study was set-up as a single center repeated measures case study, where each subject served as their own control. The recruitment of subjects, measurement methods and handling of human data were approved by the ethics committee of the University Hospitals Leuven, and written informed consent was obtained from all subjects before the start of the study. Three subjects were implanted with the Cochlear Carina Fully-Implantable Middle Ear Implant (Cochlear Ltd., Sydney, Australia; referred to as Carina system in the remainder of this paper) between November 2018 and March 2019.

² An overview of 2D skin mimicking materials is given by (Chang et al., 2018)

Table 1 lists the subject information. During implantation of the system, the skin thickness above the microphone was measured in all subjects.

The Carina system consists of the receiver coil, the implant body, the actuator, the connector and the TIM (Figure 1). It can be used in combination with a button® audio processor (BAP), an external sound processor which picks up sound on the outside of the head. When the BAP is used, the internal microphone is switched off.

The TIM of the Carina system is optimized for picking up external (speech) sounds. As it is a subcutaneous microphone, the sound that is reaching the TIM is attenuated by the skin. To compensate for the skin attenuation, the TIM has a larger diaphragm diameter. The average pre-op TIM sensitivity is displayed in Figure 3 (black dashed line). At the frequencies up to 1 kHz the TIM has an average sensitivity of -60 dB V/0.1 Pa. Above 1 kHz the sensitivity rises to its resonance peak at around 3.5 kHz, where it has an average sensitivity of about -41 dB V/0.1 Pa. Above 3.5 kHz it declines to -65 dB V/0.1 Pa at 6737 Hz.

Since 2018, a software/firmware tool from Cochlear has been available for research purposes, which allows the in-situ sensitivity of the TIM to be measured via the implant coil and the BAP. In combination with the research software the BAP serves as a reference microphone on the outside of the head. It has a sensitivity of -53 dB V/0.1 Pa $\pm$ 3 dB. When connecting to the implant via the research software, a temporary firmware is saved in the random-access memory of the Carina implant. The measurements are computed by the firmware and PC based tools. The programming of the implant is not impacted by the measurements.

In this study the in-situ sensitivity of the TIM was measured weekly, starting two weeks after surgery until 8 weeks after surgery, at which point the device was activated. Additionally, the TIM sensitivity was measured 1 month and 3 months after activation, i.e. 12 and 20 weeks ($\pm$ 1 week) after surgery, respectively. The same measurement equipment was used throughout the study.

The research software was used to record the TIM signal (internal microphone) and BAP signal (external microphone) and to calculate the TIM sensitivity:

$$TIM \text{ sensitivity [dBV/0.1 Pa]} = Mic \text{ level} - BAP \text{ level} - 53 \text{ dBV/0.1 Pa}$$

Equation 1: Calculation of TIM sensitivity

Figure 2 displays the set-up. During the measurements, the subjects sat 1 m in front of a loudspeaker (M-Audio BX5 D2) which played a white noise at 75 dB SPL for 10 seconds. This level was used as it was not too loud for the subjects and resulted in a good signal to noise ratio. The sound was recorded by the TIM using the default settings of the research software (2000 ms averaging). Additionally, the sound was recorded via the microphone of the BAP, which was attached to the head via a headband and positioned as close as possible to the TIM without touching it to avoid the BAP influencing the TIM signal. It was connected to a HiPro 2 interface (Natus Medical Denmark ApS, Taastrup, Denmark). Both interfaces were connected to a laptop running the research software.

The atmospheric pressure in Leuven was around 1000 mbar and did not fluctuate significantly. Minor pressure changes do not influence the sensitivity and could be neglected in our analysis.

The measurements were repeated four times consecutively in 5 head positions: 1. head facing the loudspeaker (*front*), 2. head turned to the side of the implant (*implanted*), 3. head turned to the non-implanted side (*non-implanted*), 4. face upwards (*up*) and 5. face downwards (*down*). To evaluate the test-retest reliability, the TIM sensitivity was remeasured in the *front* head position after removing and repositioning the headband, BAP and programming coil. This was done at two measurement sessions for each subject, i.e. test-retest data is available for each subject at two points in time.

The research software calculated the TIM sensitivity in dB V/0.1 Pa using the BAP microphone level and BAP sensitivity as reference (Equation 1). To obtain stable results, the same BAP was used at every measurement. We took photos at each measurement session to ensure that the position and orientation of the BAP and its microphone was the same for each subject for each measurement session. The TIM sensitivity was measured as root mean square (RMS) levels in 250 Hz wide frequency bands between 250 and 6000 Hz (24 bands).

For the analysis of the data, the TIM sensitivity was divided into four frequency bands. Within one frequency band the total rms level is the total of all separate band rms levels.

Figure 3 shows the mean pre-op TIM sensitivity of 62 microphones (black dashed line) and an example of an in-situ TIM sensitivity eight weeks after surgery (gray bold line). It also indicates the four frequency bands, which were chosen according to the sensitivity of the TIM: 125-1125 Hz (f1, flat frequency response), 1125 – 1875 Hz (f2, rise), 1875-4125 Hz (f3, resonance peak) and 4125-6125 Hz (f4, descent).

To answer the two research questions, we made a descriptive analysis of the TIM sensitivity changes over time for the three individual subjects. Additionally, the data was statistically interpreted analyzed using a Friedman test. The test-retest reliability was checked with a Pearson correlation.

3 Results

3.1 Test-retest reliability

The test-retest reliability was analyzed per frequency band (f1 – f4) to get a better idea of the variability of the test set-up. For this analysis, 24 sensitivity measurements were available (4 measurements in the *front* head position at 2 visits for each of the 3 subjects). First, a Pearson correlation for all test and retest measurement results was performed. There was a significant relationship between the test and retest TIM sensitivity, $r = 0.97$, $p < 0.01$. Then, the maximum absolute differences between the test and retest TIM sensitivity were calculated per frequency band. They were 0.6, 1.2, 2.1 and 3.3 dB for f1, f2, f3 and f4, respectively, i.e. the higher the frequency band, the higher the maximum absolute difference. This was also true for the mean, the standard deviation and the interquartile ranges. The maximum absolute differences per frequency band were used as cut-off values indicating clinically relevant changes in TIM sensitivity.

3.2 Pre-op versus in-situ TIM sensitivity

To answer research question 1, the individual pre-op sensitivities of the TIMs that were implanted in the three subjects were compared to the TIM sensitivities 8 weeks, 12 weeks and 20 weeks after surgery in the four frequency bands for the *front* head position (Figure 4). The sensitivity changes were very small in f1, with median pre-op to in-situ changes of 0.1 dB, -0.1 dB and -0.7 dB at 8, 12, and 20 weeks post-op. The maximal pre-op to in-situ change was 5 dB at 8 weeks post-op. Also, in f2, the changes were small with median pre-op to in-situ changes of 1.4 dB, 1.9 dB and 1.2 dB at 8, 12, and 20 weeks post-op. The maximal pre-op to in-situ change in f2 was 6.5 dB between pre-op and 20 weeks. The pre-op to in-situ sensitivity changes were highest in f3, the frequency band of the TIM resonance frequency. 8, 12, and 20 weeks after surgery the sensitivities were 7.1 dB, 5.4 dB and 4.3

dB lower, respectively, compared to the pre-op sensitivity. There seems to be a trend towards a lower discrepancy to the pre-op sensitivity with a longer timeframe between surgery and the in-situ measurement in f3. The maximal pre-op to in-situ sensitivity change in f3 was 15 dB, 12 weeks after surgery. In f4, the sensitivity differences were also very small with median changes of -0.1 dB, 0.9 dB and 2.3 dB in week 8, 12, and 20, respectively. The maximal difference was 4.7 dB in week 20.

A Friedman analysis was done, which did not reveal any significant differences between pre-op and 8 weeks, 12 weeks and 20 weeks post-op in-situ sensitivity ($p > 0.05$) in this small sample group.

Figure 5 shows the individual pre-op TIM sensitivities (black solid lines) and the individual in-situ sensitivities (gray dotted lines) of the three subjects 20 weeks after surgery in the *front* head position for the entire frequency range. All subjects showed a clear resonance peak around 3 kHz 20 weeks after surgery. At first sight it is obvious, that there are discrepancies between the individual pre-op and in-situ TIM sensitivities. The in-situ TIM sensitivity of S1 (Figure 5A) is close to the pre-op TIM sensitivity at most frequencies, except at the resonance frequency of the TIM, where it is approximately 3 dB lower than the pre-op sensitivity. In this patient, the real resonance peak of the TIM cannot be seen in the pre-op measurement due to the low resolution of the measurement. The TIM of S2 (Figure 5B) is approximately 3 dB more sensitive compared to the pre-op TIM sensitivity at 0.5 kHz, shows a dip of approximately 4 dB at 1.5 kHz and then follows the mean TIM sensitivity up to 3 kHz. At the pre-op resonance frequency (~3.5 kHz), the in-situ TIM sensitivity of S2 shows a large dip, which leads to a big discrepancy (~20 dB) between both sensitivities. The TIM of S3 (Figure 5C) shows the highest discrepancy to the pre-op TIM sensitivity, mainly in the frequency region of the TIM resonance (~14 dB at 3 kHz). It also shows a dip at 1.5 kHz (~6 dB).

3.3 In-situ TIM Sensitivity over time

Figure 6 shows the mean TIM sensitivity (average of four consecutive measurements) ± 1 SD for all subjects and all head positions across time (2 – 20 weeks after implantation) divided into four frequency bands (f1 – f4). It gives an overview of all study results at a glance. In Figure 7 we have combined all subjects and all head positions to display the absolute sensitivity changes between consecutive weeks as box-whisker plots per frequency band (f1-f4). In the following we first discuss Figure 6 in more detail.

In f1 the TIM sensitivity was similar over time for all three subjects. The TIM of S2 was approximately 5 dB more sensitive compared to the TIMs of S1 and S3. The mean absolute TIM sensitivity change between two consecutive weeks for all subjects and head positions was 0.6 dB with a range from 0.0 dB (S1, weeks 6-7 in head position *implanted*) to 2.4 dB (S3, weeks 6 and 7 in head position *implanted*). The interquartile range for f1 was 0.5 dB (refer to Figure 7). The mean absolute sensitivity change was equal to the cut-off value of 0.6 dB (defined in section 3.1). 60% of the absolute changes between consecutive weeks in f1 were below this cut-off value.

In f2 the TIM sensitivity was still quite similar over time in most head positions for S1 and S2. The TIM sensitivity of S3 showed some more variability. The TIM of S2 was approximately 5 dB more sensitive compared to the TIMs of S1 and S3 only in head positions *non-implanted* and *up*, in the other head positions it was similar for all subjects. The mean absolute TIM sensitivity change between two consecutive weeks for all subjects and head positions was 1.1 dB with a range from 0.0 dB (S1, weeks 3-4 in head position *implanted*) to 4.8 dB (S1, weeks 8-12 in head position *down*). The interquartile range was 1.3 dB (refer to Figure 7). The mean absolute sensitivity change was smaller than the cut-off value of 1.2 dB. 61% of the absolute changes between consecutive weeks in f2 were below this cut-off value.

Of the four frequency bands under investigation, f3 showed the highest TIM sensitivity but also the highest variability in TIM sensitivity over time. The TIM of S2 was most sensitive in nearly all weeks and head positions. While the TIMs of S1 and S3 had a similar sensitivity over time in f1 and f2, the TIM sensitivity of S3 is lowest in f3 for all weeks and head positions, except for head position *down*. The mean absolute TIM sensitivity change between two consecutive weeks for all subjects and head positions was 1.9 dB with a range from 0.0 dB (S1, weeks 2-3 in head position *implanted*) to 7.9 dB (S1, weeks 8-12 in head position *non-implanted*). The interquartile range was 1.8 dB (refer to Figure 7). The mean absolute sensitivity change was smaller than the cut-off value of 2.1 dB. 68% of the absolute changes between consecutive weeks in f3 were below this cut-off value.

In f4 the TIM sensitivity is highest for S2 in most head positions. For the *front* head position the TIM sensitivity was quite similar over time for S1 and S2. In the other head positions, there was more variability in the TIM sensitivity. The mean absolute TIM sensitivity change between two consecutive weeks for all subjects and head positions was 2.3 dB with a range from 0.0 dB (S1, weeks 5-6 in head position *implanted*) to 12.2 dB (S2, weeks 8-12 in head position *implanted*). The interquartile range was 2.1 dB (refer to Figure 7). The mean absolute sensitivity change was smaller than the cut-off value of 3.3 dB. 75% of the absolute changes between consecutive weeks in f4 were below this cut-off value.

We performed a Friedman's ANOVA on the data per frequency band and per head position to test if statistically significant TIM sensitivity changes occurred over time. There were no significant differences between any of the weeks in any of the four frequency bands for any of the head positions, except for f3 when the head was turned to the non-implanted ear ($\chi^2 = 16.178$, $p < 0.05$). To create the test statistic, the data is ranked per subject, so differences in the baseline sensitivity between subjects should not influence the test statistic. However, due to the low number of subjects, the power is very low, and the data is probably not distributed like a chi-square distribution. Therefore, the results of Friedman's ANOVA must be interpreted with care. As there was a significant difference found for f3, a Wilcoxon test was performed between the groups with the highest (12 weeks) and lowest (5 weeks) ranks, but the difference between the TIM sensitivities between those two weeks was not significant ($p > 0.05$).

In Figure 7 we have combined all subjects and all head positions to display the absolute sensitivity changes between consecutive weeks as box-whisker plots per frequency band (f1-f4). The mean absolute sensitivity changes (and interquartile ranges) for f1, f2, f3 and f4 were 0.5 (0.6) dB, 1.1 (1.2) dB, 1.7 (1.8) dB and 2.0 (2.2) dB, respectively. They were all smaller than the cut-off values for a clinically significant change (defined in section 3.1).

On this dataset we performed a Friedman's ANOVA to test if there is a statistically significant difference in the absolute TIM sensitivity changes between frequency bands. There was a significant overall effect of frequency band ($\chi^2 = 76.889$, $p < 0.01$). Wilcoxon signed-rank tests were used to follow up on this finding. A Bonferroni correction was applied so all effects are reported at a 0.0125 level of significance. It appeared that there was a significant difference in the absolute sensitivity changes between all frequency bands ($p < 0.0125$), except between f3 and f4 ($p > 0.0125$).

In summary, the data displayed in Figure 7 showed that the lower the frequency band, the lower the absolute sensitivity changes between consecutive weeks, the lower the variability and the lower the maximum absolute sensitivity change.

Table 2 shows the mean absolute sensitivity changes between week 2 and weeks 8, 12 and 20, respectively, averaged over all subjects for the *front* head position. Comparing the sensitivities at week 2 and week 8 (activation), the mean absolute sensitivity change between weeks was in the

range between 0.6 dB (f2) and 1.5 dB (f3). All changes but the one in f1 were smaller than the cut-off values defined in section 3.1, thus not clinically relevant. Between weeks 2 and 12, the mean absolute sensitivity changes between weeks for the four frequency bands were in the range between 0.4 dB (f1) and 1.4 dB (f2). All changes but the one in f2 were smaller than the cut-off values. The mean absolute sensitivity changes for the longest evaluation period (between weeks 2 and 20) were between 0.7 dB (f1) and 1.6 dB (f3 and f4). All changes but the one in f1 were smaller than the cut-off values.

We performed a Wilcoxon signed-rank test on this dataset and found no statistically significant differences between week 2 and week 8, week 2 and week 12, and week 2 and week 20 in any of the four frequency bands ($p > 0.05$).

4 Discussion

The discrepancies between the individual pre-op and in-situ TIM sensitivities 20 weeks after surgery were shown in Figure 5. All three subjects showed a different in-situ TIM sensitivity and the discrepancies to the pre-op sensitivity varied among subjects. The TIM sensitivity is a very important input parameter for the fitting process of the AMEI to the hearing loss of the patient. If the in-situ TIM sensitivity is lower or higher than what the fitting software expects, it can affect the gain and maximum power output set in the fitting software, which, in turn, can have an influence on the subject's speech performance.

In S1, the in-situ sensitivity aligned well with the pre-op sensitivity except for the area of the resonance peak. In that area, there was a minor discrepancy, which should not influence the gain settings significantly. However, for S2 and S3, the discrepancies were much higher and were not limited to the area of the resonance peak. An influence on the gain settings could have been expected, which potentially also influenced the speech discrimination. One possibility to avoid using a wrong TIM sensitivity as input parameter for the fitting process would be to measure the individual in-situ sensitivity as part of the fitting process and to use this individual in-situ sensitivity as input parameter for the gain and maximum power Output calculations in the fitting software.

The TIM sensitivity of S3 around 3 kHz was approximately 14 dB below the mean pre-op TIM sensitivity. The sensitivity in f3 was lowest in all head positions compared to the other two subjects while it was nearly the same as for S1 in f1 and f2. One reason for that could be the thicker skin of that subject (7 mm compared to 4 mm for the other two subjects). A thicker skin means more attenuation by the skin and more mass on the microphone membrane which should move the resonance frequency downwards.

A major finding of this research is thus that the in-situ TIM sensitivity varied between subjects and differed considerably compared to the individual pre-op TIM sensitivity. One possible reason for that could be the individual biomechanical characteristics of the subject's skin, such as the skin tension or skin density.

The individual TIM sensitivity changes over time were shown for all head positions and frequency bands in Figure 6.

In f1 (125-1125 Hz) the TIM sensitivity curves were flat over time for all head positions, i.e. there was no clinically relevant difference from week to week. The TIM of S2 was approximately 5 dB more sensitive than the TIMs of the other two subjects. One potential reason for that could be a different skin thickness, but this is unlikely given the fact that this subject presented similar skin thickness as S1 (4 mm) during surgery. Even a change in skin thickness after surgery, e.g. by scar tissue, is not

likely to cause a sensitivity change of 5 dB in f1 as simulations show that the skin thickness does not change the microphone sensitivity below 1 kHz (information received from the manufacturer of the AMEI).

In f2 (1125 – 1875 Hz), the sensitivity curves were also relatively flat over time, especially when the head was turned to the non-implanted ear, i.e. when there was more skin tension above the TIM. The TIM sensitivity curves of S2 were closer to the TIM sensitivity curves of the other two subjects in head positions *front*, *implanted* and *down*. One reason for that could be the fact that S2 showed a dip in the sensitivity at 1.5 kHz for these three head positions, even 20 weeks after implantation (refer to Figure 5). This dip at 1.5 kHz was most pronounced when the head was turned to the implanted ear, i.e. when there was less skin tension above the microphone. This explains why for this head position the TIM sensitivity was below the TIM sensitivity of the other two subjects, while it was most sensitive for the head positions *non-implanted* and *up* for this subject. In the area of the dip, the in-situ sensitivity was up to 10 dB lower than the pre-op TIM sensitivity. When the head was turned to the non-implanted ear, i.e. more skin tension above the TIM, this dip at 1.5 kHz disappeared. We could not see this effect in the other two subjects. This subject had a smaller head than the other two subjects (not measured, only observed), but the skin thickness was the same as in S1 during surgery. We did not measure skin thickness after implantation in this subject and we also did not measure skin tension in our study at any point and therefore cannot support our hypothesis with data. However, we hypothesize that the dip around 1.5 kHz in S2 was related to skin tension above the microphone.

In f3 (1875 – 4125 Hz) the TIM sensitivity was highest for all subjects compared to the other frequency bands. This is because the resonance peak of the TIM is located in this frequency range (~3.5 kHz, refer to Figure 3). In this frequency band, there was also the largest deviation from the pre-op TIM sensitivity and the largest SD from the mean TIM sensitivity. In general, this could mean that the implantation and the healing process have the largest influence on the in-situ TIM sensitivity around the resonance frequency of the TIM.

In f4 (4125 – 6125 Hz) the TIM sensitivities had the second most variability of the four frequency bands. For most weeks and head positions, the TIM of S2 is most sensitive in f4. Opposite to the other three frequency bands, the difference in f4 between the pre-op and in-situ sensitivity got bigger with time.

The research software is a good tool to measure the in-situ sensitivity of the TIM in subjects implanted with the Carina system. The measurements done with the software have a good test-retest reliability, which was best in f1. The TIM sensitivity measurements can be influenced by the exact BAP position and orientation. To minimize this influence, for clinical purposes, we would like to suggest, that there should be a possibility to calibrate the BAP before the measurements via the research software to prevent BAP level variability to influence the measurement outcomes. A template with the desired distance between the TIM and the BAP microphone, which can be applied to the BAP might also be helpful to reduce the set-up related variability in measurements. Small fluctuations over time can be explained by BAP microphone and TIM level differences due to a slightly variable BAP-TIM distance and relative position and orientation. In general, the research software is a good and reliable tool to measure the in-situ TIM sensitivity in subjects implanted with the Carina system.

5 Conclusion

This study investigated TIM sensitivity changes over time measured with a research software in subjects implanted with a fully-implantable AMEI. The TIM sensitivity changed after implantation with clinically relevant changes around the resonance frequency of the TIM. Based on our results, it is essential to measure the in-situ TIM sensitivity at the initial fitting of the AMEI, as it has an influence on the available gain and output. Our mid-term data suggests no clinically relevant changes over time in TIM sensitivity in any of the four investigated frequency bands with a clear decrease in variability over time. Finally, changes in the in-situ TIM sensitivity between various head positions have been measured, demonstrating the need for sensitivity testing in different head positions as part of the fitting process. Prospective gathering of more TIM sensitivity data with the research software would be useful.

6 Acknowledgements

We would like to thank Katleen de Voecht from UZ Leuven for her audiological support and Joris Walraevens and Stijn Eeckhoudt from Cochlear for the technical input.

7 Funding

This work was supported by the Flanders Innovation and Entrepreneurship [grant number IWT140265] and Cochlear Ltd. (Sydney, Australia)

8 References

- Banakiss Hartl, R.M., Easter, J.R., Alhussaini, M., Benichoux, V., Tollin, D.J., Jenkins, H.A., 2017. Air- and Bone-Conducted Sources of Feedback with an Active Middle Ear Implant.
- Bruschini, L., Berrettini, S., Forli, F., Murri, A., Cuda, D., 2016. The Carina middle ear implant: surgical and functional outcomes. *Eur. Arch. Oto-Rhino-Laryngology* 273, 3631–3640. <https://doi.org/10.1007/s00405-016-3998-1>
- Bruschini, L., Forli, F., Santoro, A., Bruschini, P., Berretini, S., 2009. Fully implantable Otologics MET Carina TM device for the treatment of sensorineural hearing loss. Preliminary surgical and clinical results. *Acta Otorhinolaryngol. Ital.* 29, 79–85.
- Calero, D., Paul, S., Gesing, A., Alves, F., Cordioli, J.A., 2018. A technical review and evaluation of implantable sensors for hearing devices. *Biomed. Eng. Online* 17, 1–26. <https://doi.org/10.1186/s12938-018-0454-z>
- Chang, T., Li, K., Yang, H., Chen, P., 2018. Multifunctionality and Mechanical Actuation of 2D Materials for Skin-Mimicking Capabilities. *Adv. Mater.* 30, 1–13. <https://doi.org/10.1002/adma.201802418>
- Firooz, A., Zartab, H., Pazhohi, N., Fanian, F., Janani, L., 2017. The influence of gender and age on the thickness and echo-density of skin 13–20. <https://doi.org/10.1111/srt.12294>
- Gamm, U.A., Grossöhmichen, M., Salcher, R.B., Prenzler, N.K., Lenarz, T., Maier, H., 2019. Optimum Coupling of an Active Middle Ear Actuator : Effect of Loading Forces on Actuator Output and Conductive Losses. *Otol. Neurotol.* 40, 789–796. <https://doi.org/10.1097/MAO.0000000000002253>
- Grossöhmichen, M., Waldmann, B., Salcher, R., Prenzler, N., Lenarz, T., Maier, H., 2017. Validation of methods for prediction of clinical output levels of active middle ear implants from measurements in human cadaveric ears. *Sci. Rep.* 7, 15877. <https://doi.org/10.1038/s41598-017-16107-9>
- Kraus, E.M., Shohet, J. a, Catalano, P.J., 2011. Envoy Esteem Totally Implantable Hearing System: phase 2 trial, 1-year hearing results. *Otolaryngol. Head. Neck Surg.* 145, 100–109. <https://doi.org/10.1177/0194599811401709>
- Lefebvre, P.P., Gisbert, J., Cuda, D., Tringali, S., Deveze, A., 2017. A retrospective multicentre cohort review of patient characteristics and surgical aspects versus the long-term outcomes for recipients of a fully implantable active middle ear implant. *Audiol. Neurotol.* 21, 333–345. <https://doi.org/10.1159/000454666>
- Lewis, J., 2012. Understanding Microphone Sensitivity. *Analog Dialogue* 46, 1–3.
- Martin, C., Deveze, A., Richard, C., Lefebvre, P.P., Decat, M., Ibañez, L.G., Truy, E., Mom, T., Lavieille, J.-P., Magnan, J., Dubreuil, C., Tringali, S., 2009. European results with totally implantable carina placed on the round window: 2-year follow-up. *Otol. Neurotol.* 30, 1196–1203. <https://doi.org/10.1097/MAO.0b013e3181c34898>
- Maurer, J., Savvas, E., 2010. The Esteem system: A totally implantable hearing device. *Adv. Otorhinolaryngol.* 69, 59–71. <https://doi.org/10.1159/000318523>
- Mylanus, E.A.M., Snik, A.F.M., Cremers, C.W.R.J., 1994. Influence of the Thickness of the Skin and Subcutaneous Tissue Covering the Mastoid on Bone-conduction Thresholds Obtained Transcutaneously versus Percutaneously. *Scand. Audiol.* 23, 201–203. <https://doi.org/10.3109/01050399409047509>

- Peixoto, C., Miranda, C., Bento, M., Oliveira, S., Pratas, R., Correia, V., 2019. The first results of a totally implanted active middle ear device. *Eur. Arch. Oto-Rhino-Laryngology*.
<https://doi.org/10.1007/s00405-019-05557-8>
- Pulcherio, J.O.B., Bittencourt, A.G., Burke, P.R., Monsanto, R.D.C., de Brito, R., Tsuji, R.K., Bento, R.F., 2014. Carina® and esteem® : a systematic review of fully implantable hearing devices. *PLoS One* 9, e110636. <https://doi.org/10.1371/journal.pone.0110636>
- Savaş, V.A., Gündüz, B., Karamert, R., Cevizci, R., Düzlü, M., Tutar, H., Bayazit, Y.A., 2016. Comparison of Carina active middle-ear implant with conventional hearing aids for mixed hearing loss. *J. Laryngol. Otol.* 130, 340–343. <https://doi.org/10.1017/S0022215116000748>
- Siegert, R., Mattheis, S., Kasic, J., 2007. Fully implantable hearing aids in patients with congenital auricular atresia. *Laryngoscope* 117, 336–340.
<https://doi.org/10.1097/MLG.0b013e31802b6561>
- Uhler, K., Anderson, M.C., Jenkins, H.A., 2016. Long-Term Outcome Data in Patients following One Year's Use of a Fully Implantable Active Middle Ear Implant. *Audiol. Neurotol.* 21, 105–112.
<https://doi.org/10.1159/000444243>
- Wagner, F., Todt, I., Wagner, J., Ernst, A., 2010. Indications and Candidacy for Active Middle Ear Implants, in: *Active Middle Ear Implants*. *Adv Otorhinolaryngol*, Karger, 69, 20–26.
- Zenner, H., Rodriguez Jorge, J., 2010. Totally implantable active middle ear implants: Ten Year's Experiencie at the University of Tuebingen, *Adv Otolaryngology*. 69, 72-84.

A

B

White Noise
75 dB SPL -
10s

Figure Captions

Figure 1: The Cochlear Carina System including the implant body, the receiver coil, the microphone/TIM, the actuator and the connector (A). Optionally, a button audio processor can be used in combination with the Carina system. B shows the TIM in-situ under the skin and fixed to the skull-bone. Courtesy of Cochlear Ltd.

Figure 2: Measurement set-up with loudspeaker, headband, BAP, Programming Coil, HiPro, Carina Interface and Laptop running the research software

Figure 1: Mean pre-op TIM sensitivity of 62 microphones (black dashed line) and mean in-situ TIM sensitivity measured in S1 in the front head position eight weeks after surgery shown as 24 rms levels (gray bold line). The error bars represent 1 standard deviation of 4 consecutive measurements. For analysis, the 24 rms levels were combined to 4 frequency bands: f1: 125-1125 Hz, f2: 1125-1875, f3: 1875-4125 Hz, f4: 4125 - 6125

Figure 2: Change in microphone sensitivity between two measurements (pre-op vs 8, 12, and 20 weeks post-op in the front head position) for the four frequency bands, averaged over 3 subjects

Figure 5: Individual pre-op (black solid line) and 20 weeks post-op (gray dotted line) TIM sensitivity of S1 (A), S2 (B) and S3 (C)

Figure 6: Mean microphone acoustic sensitivity (n=4) for all weeks for each individual subject for the four frequency bands (f1-f4) for all head positions. The error bars represent 1 standard deviation

Figure 7: Absolute sensitivity changes between consecutive weeks for the four frequency bands (f1-f4) for all subjects and head positions. The circles indicate outliers.

Tables

Subject ID	Gender	Age at implantation [years]	Side of implantation	Skin thickness [mm]
S1	Female	57	Right	4
S2	Male	62	Left	4
S3	Male	53	Right	7

Table 1: Subject information

Mean absolute sensitivity change between weeks	f1 [dB]	f2 [dB]	f3 [dB]	f4 [dB]
2 and 8 (activation)	0.8	0.6	1.5	1.2
2 and 12 (1 month after activation)	0.4	1.4	0.8	1.1
2 and 20 weeks (3 months after activation)	0.7	0.8	1.6	1.6

Table 2: Absolute sensitivity changes between week 2 and weeks 8, 12 and 20, respectively, averaged over all subjects for the front head position