RESEARCH PROTOCOL

Long term follow-up of the Ponto Wide implant: 10 years of clinical evaluation.

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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

BAHI	**Bone-anchored hearing implant**
ISQ	**Implant stability quotient**
CTc	**Central Ethics Review Committee / Centrale ethische Toetsingscommissie (Dutch)**
IC	**Informed consent**
IOI-HA	**International Outcome Inventory for Hearing Aids**
LIT-TR	**Linear incision technique with tissue reduction**
LIT-TP	**Linear incision technique with tissue preservation**
pBCD	**Percutaneous Bone Conduction Device**
tBCD	**Transcutaneous Bone Conduction Device**
APHAB	**Abbreviated Profile of Hearing Aid Benefit**
GBI	**Glasgow Benefit Inventory**
GCP	**Good Clinical Practice**

SUMMARY

Rationale: Since the introduction of the bone-anchored hearing implant (BAHI) in 1977 (1), implants have evolved over the years. The implant design has changed, resulting in wider diameter implants. In 2011, the 4.5-mm-wide implant was introduced. This implant has a larger contact surface between the implant and the bone compared to prior implants. Previous studies have shown that there is a high survival rate with the use of the 4.5-mm-wide implant at 6 months and 3 years after implantation (2, 3). Similar results were observed for a follow-up duration of 5 years (4). While the outcomes for this duration are positive, there is limited data available concerning the long-term follow-up duration (>10 years) of the 4.5-mm-wide implant.

Objective: The primary objective is to investigate the survival of the Ponto Wide Implant at least 10 years after implantation.

Study design: A single center, prospective study with a single follow-up visit performed at least 10 years after Ponto Wide implantation. This study is a continuation of previously conducted clinical trials of which 6-months, 3- years and 5-years results have been published (3-7).

Study population: The study population consists of patients with a Ponto Wide implant (diameter 4.5mm, length 4.0mm) previously participating in one of two already completed studies (3, 7).

Main study parameter: The main parameter is implant survival and will be assessed at least 10 years after implantation.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The study consists of a single follow-up visit. Except for an additional check-up, there will be no further benefit to participating in the study. Since the follow-up visit is comparable to a regular visit and does not involve any invasive procedures, there are also no risks associated with participating in the study.

1. INTRODUCTION AND LITERATURE REVIEW

1.1 Background

Percutaneous bone-anchored hearing implants have been used for patients with conductive hearing loss, mixed hearing loss, and single-sided deafness since their introduction in 1977 (1). The percutaneous implant is placed in the temporal bone behind the ear. Sound is detected by the vibrating bone conduction device and transmitted through the implant to the postauricular temporal bone, eventually reaching the cochlea. The implant penetrates through the skin, forming the connection between the vibrating bone conduction device and the postauricular temporal bone (1). Critical to the proper functioning of a percutaneous implant is the creation of a reaction-free cutaneous-implant junction (8). Research on dental implants has shown that the metal titanium is highly suitable as an implant, as it is well tolerated by the body (9). Several follow-up studies with titanium implants outside the oral cavity ensued. Research showed a permanent and reaction-free rigid penetration of the skin (1, 10). As a result, it can be concluded that titanium can also be used in other bones of the body (11), such as the temporal bone in case of a percutaneous bone-anchored hearing implant.

However, despite the use of titanium implants other complications emerged, including skin reactions, infections, and skin growth over the abutment (12-14). These complications, as well as failure of osseointegration, can lead to loss of the hearing implant. Over the years, various adjustments have been made to surgical techniques and implant design to minimize the risk of complications and ensure optimal osseointegration. Subtle changes in shape, length, and width of dental implants were found to influence success rates (15). The use of wide-diameter implants facilitates increased bone-to-implant contact (16) resulting in higher implant stability and survival (17). In 2011, titanium hearing implants with a wider diameter were introduced: the 4.5-mm-wide implant. This implant, which has increased in diameter by 0.75 mm, resulted in higher implant survival rates compared to previous designs (2, 18). Oticon Medical, one of the producers of percutaneous bone-anchored hearing implants, introduced their wider-diameter implant in 2011: the Ponto Wide implant. Subsequent studies in the following years have shown a high survival rate with the use of the 4.5-mm-wide implant at 6 months, 3 years, and 5 years after implantation (2-4). Similar positive outcomes were observed when examining implant stability. Although these outcome measures appear positive within a 5-year duration post-implantation, this study examines various outcome measures of the Ponto Wide implant during long-term follow-up of at least 10 years.

2. OBJECTIVES

2.1 Primary objective

The primary objective is to investigate the survival of the Ponto Wide Implant at least 10 years after implantation.

2.2 Secondary objectives

1. To determine the amount and causes of implant loss and implant and/or abutment removal.
2. To establish the stability of the implant.
3. To assess skin complications.
4. To investigate daily usage and the number of hours of use of the sound processor.
5. To determine the quality of life.

2.3 Hypothesis

Regarding this study, it is hypothesized that the survival of the implant will be equal to the implant survival at 6 months, 3 years, and 5 years after implantation.

3. STUDY DESIGN

3.1 Duration of study

Given that it is a study with a single follow-up visit, a study duration of 3-6 months is expected. All patients who participated in one of the two previously published studies will be approached (3, 7). The inclusion of patients will start after approval from the Central Ethics Review Committee and will take place within one month. After obtaining approval, a physical appointment is scheduled for all patients who agree to participate in the study to conduct the measurements. The expected end date of the study will be between the end of 2024 and March 2025.

3.2 Study design

All patients who participated in the previously published studies (3, 7) will be screened through their medical files to determine if there has been any implant loss, implant and/or abutment removal, or if they have passed away. If this information is not documented, patients will be contacted. Interested patients will receive information about the study, after which they will have a two-week period to consider their participation. When informed consent (IC) is obtained, the patient's medical file will be reviewed for baseline characteristics and a physical appointment will be scheduled. During this physical appointment, various variables are measured and patients are asked to complete two questionnaires. If the patient is unable to attend a physical follow-up visit but still willing to participate, a telephone appointment will be scheduled. In this way, experiences regarding the implant, wearing the sound processor, and quality of life can still be obtained.
The telephone questions are described in section 5.2.8. An overview of how the variables will be obtained is shown in Table 1.

Table 1. Obtaining the variables during the study

	Patient file	Single follow up visit	Phone call
Baseline characteristics	**X**		
Implant removal	**X**	**X**	**X**
Implant loss	**X**	**X**	**X**
ISQ measurement		**X**	
Skin status		**X**	
IPS-score		**X**	
Use of sound processor		**X**	**X**
Quality of life		**X**	**X**
Hearing status	**X**	**X**	

4. STUDY POPULATION

The study population consists of patients with a Ponto Wide implant (diameter 4.5mm, length 4.0mm) who previously participated in one of two already conducted and completed studies (3, 7).

4.1 Inclusion criteria

1. Implantation with Ponto Wide implant (diameter 4.5 mm, length 4.0 mm)
2. Ten or more years of post-operative follow-up.
3. Valid informed consent

Based on the inclusion criteria, there is a maximum of 64 available patients that can be included.

4.2 Exclusion criteria

No specific exclusion criteria have been set for the study.

5. INVESTIGATIONAL PRODUCT

5.1 Ponto Wide Implant

In this study we want to investigate the long-term survival of the Ponto Wide implant (diameter 4.5mm, length 4.0mm, Oticon Medical AB, Askim, Sweden).

The Ponto Wide implant has a wider diameter and a different cutting geometry and threading compared to previous implants. Ponto abutments of lengths 6, 9, and 12 mm were used, depending on skin thickness.

6. METHODS

6.1 Study endpoints

6.1.1 Primary study endpoint

Implant survival of the Ponto Wide Implant at least 10 years after implantation.

6.1.2 Secondary study endpoints

- Evaluation of reasons for implant loss and implant and/or abutment removal.
- Implant stability at >10-year follow-up .
- Skin complication rates at >10-year follow-up.
- Average sound processor usage (hours per day; days/week) >10 years post-surgery.
- Glasgow Benefit Inventory (GBI) scores >10 years post-surgery
- International Outcome Inventory for Hearing Aids (IOI-HA) score >10 years post-surgery

Demographics and (baseline) variables:

- Gender
- Age at surgery
- Etiology of hearing loss at surgery
- Ethnical background
- Type of surgery
    - Linear incision technique with tissue reduction (LIT-TR)
    - Linear incision technique with tissue preservation (LIT-TP)
- Revision surgery (skin revision, abutment change, re-implantation)
- Type and length of abutment
- Indication left/right ear
- Time since surgery (follow-up)

6.2 **Study procedures**

6.2.1 **Investigation outline**

Patient inclusion involves actively approaching patients who participated in one of the two previously published studies (3, 7). If it is known in advance that a patient has experienced implant loss or has passed away, they will not be contacted. Interested patients will receive information about the study, after which they will have a two-week period to consider their participation. When informed consent (IC) is obtained, a physical appointment is scheduled. During this physical appointment, various variables are measured and patients will be asked to complete two questionnaires. If the patient is unable to attend a physical follow-up visit, a telephone appointment will be scheduled. All data will be stored on a secured network drive.

6.2.2 **Long term survival of implant**

All patients will be asked if they have experienced any implant-related problems that could have affected the longevity of the implant in the last 5 years. If implant loss and implant and/or abutment removal has occurred, the number of implants/abutments involved and the time between implantation and the event will be noted. Additionally, the reason for implant removal and the most likely cause of implant loss will be documented.

6.2.3 **Implant stability Quotient (ISQ)**

ISQ will be measured at the visit. The resonance frequency analysis renders an ISQ value ranging from 1 to 100. Measurements shall be performed at the abutment level. Perpendicular measurements result in two values, where the lowest and highest values are recorded as an ISQ-low value and an ISQ-high value, respectively. The measurement should preferably be done by the same Osstell instrument (Osstell, Gothenburg, Sweden) that was used in the previous completed study. SmartPeg 55 will be used during the measurement (Osstell, Gothenburg, Sweden).

6.2.4 **Holgers' classification**

The Holgers classification shows different grades of inflammation of the skin around the titanium abutments (19). The skin will be assessed during a visit according to the Holgers classification. The following adjusted scale will be used:

0. No irritation. Epithelium debris removed if present.
1. Slight redness, local treatment.
2. Red and slightly moist tissue. No granuloma formation noted. Local treatment. Extra controls.
3. Status as in 1 and 2 but local revision became necessary

4. Removal of skin-penetrating implant necessary due to infection.

R Removed implant for reasons not related to skin problems.

6.2.5 **IPS-score**

The Holgers' classification has long been used to report on soft tissue reactions around percutaneous implants for bone conduction devices (BCDs). However, in addition to signs of inflammation/infection of the skin around the abutment, other parameters have also shown important. The IPS score was therefore developed to include also parameters such as pain and skin height (20). Moreover, the IPS scoring system can be used not only for percutaneous bone conduction devices (pBCD) but also for transcutaneous bone conduction devices (tBCD). Depending on the IPS score, a treatment recommendation is provided. The IPS-score must be completed during the physical appointment The skin around the implant will be assessed based on the following components:

1. Inflammation:

- Skin Integrity (intact = 0 / not intact = 1)
- Erythema (none = 0 / present = 1)
- Edema (none = 0 / present = 1)
- Granulation tissue formation (none = 0/ present = 1)

2. Pain:

- None = 0
- Present, but no increase during manipulation abutment AND <6 wks present = 1
- Present, and increase during manipulation abutment AND/OR >6 wks present = 2

3. Skin height:

- Normal = 0
- Increased, but able to couple sound processor = 1
- Above rim abutment/unable to couple sound processor =2

The IPS-scale offers a standardized treatment advice for each IPS-scale:

- $I_{0-1}P_0S_{0-1}$ = no treatment
- $I_0P_1S_{0-1}$ = no treatment
- $I_1P_1S_{0-1}$ = local topical treatment
- $I_{2-3}P_{0-1}S_{0-1}$ = local topical treatment
- $I_{0-4}P_2S_{0-1}$ = consider adding systemic treatment for possible peri-implantitis

- $I_{0\text{-}4}P_{0\text{-}2}S_2$ / $I_4P_{0\text{-}1}S_0$ = consider revision/removal surgery or longer abutment (in combination with antibiotic treatment depending on I and P-score)

During a visit, both the Holgers classification and the IPS score will be used to allow for the best possible comparison with previously published studies.

6.2.6 Daily usage and the number of hours of use of the sound processor

All patients will be asked if they wear their sound processor daily and for how many hours per day and how many days per week. Additionally, patients will be asked if they experience or previously have experienced any deficiencies or complaints regarding the sound processor and whether the sound processor has been replaced in the past. The brand and model number of the sound processor will be recorded.

6.2.7 Quality of life

Patients are asked if they want to complete two questionnaires regarding their hearing-related quality of life.

The International Outcome Inventory for Hearing Aids (IOI-HA) is a seven-item questionnaire designed to be generally applicable in evaluating the effectiveness of hearing aid treatments (21). These questions provide understanding into how satisfied patients are with their hearing aid. Additionally, patients are asked to complete the Glasgow Benefit Inventory (GBI) questionnaire (22). This questionnaire is used to evaluate the quality of life after a medical intervention. The questionnaire consists of 18 items that correspond to different aspects of the patient's well-being: quality of life, self-confidence, support, general health, and social involvement.

6.2.8 Phone call

The outcomes of all the above variables will be obtained during a physical consultation. If this is not possible, attempts will be made to contact the patient by phone and ask the following questions:

- ‘Is the abutment still in place?’
- ‘Do you use the sound processor daily?’ If this is not the case, ‘What is the reason you do not wear the sound processor daily?’
- ‘How many hours per day do you use the sound processor?’

- ‘How many days per week do you use the sound processor?
- ‘Do you, or have you previously, experienced any deficiencies or complaints?’
- ‘Has the sound processor been replaced in the past due to upgrades or possible problems?’
- Has the implant, along with the sound processor, improved your quality of life compared to not using them?

6.2.9 **Withdrawal of individual subjects**

Subjects can leave the study at any time for any reason if they wish to do so without any consequences

7. STATISTICAL ANALYSIS

All patients from the previous investigations will be asked to participate. Therefore, no sample size calculation was performed. The Wilcoxon signed-rank test will be used to analyze changes within groups over time. Implant survival will be analyzed using a Kaplan-Meier survival curve. A significance level of 0.05 will be used and the test will be two-tailed.

8. ETHICAL CONSIDERATIONS

8.1 Regulation statement

The investigation will be conducted in accordance with applicable local regulations, e.g. data protection legislation. Valid informed consent will be ensured before data collection and inclusion. Due to the nature of this study, a written approval of the local Ethics Committee is necessary. The study will not start until approval from the Ethics Committee is obtained. This investigation will be conducted in accordance with the ISO 14155, the ethical principles as described in the latest version of the Declaration of Helsinki, and Good Clinical Practice (GCP). The study will be registered at ClinicalTirals.gov.

8.2 Recruitment and consent

All patients who have participated in one of the two previously completed studies (3, 7) are eligible to take part in the study and will be contacted. Information about the study will be sent to the potential study participant, after which they will have a two-week period to consider their participation. If patients are willing to participate after the consideration period, the informed consent form will be signed by both the patient and the researcher.

8.3 Benefits and risks assessment, group relatedness

The study consists of a single follow-up visit. Except for an additional check-up, there will be no further benefit to participating in the study. Since the follow-up visit is comparable to a regular visit and does not involve any invasive procedures, there are also no risks associated with participating in the study.

9. ADMINISTRATIVE APSECTS AND PUBLICATION

9.1 Handling and storage of data and documents

Data will be captured in an electronic data capture (EDC) system using electronic case report forms (eCRFs). Patient information (i.e., name, initials, birth date) will be manually processed and stored on a secured network that requires a code for access. All data obtained during the study period will be stored for 15 years after the completion of the study.

9.2 Publication

The result of this investigation will be submitted (aiming to publish) into a peer-reviewed journal and for presentation at relevant conference(s).

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