Clinical investigation plan

Title: Single center evaluation of a sound processor for a transcutaneous system

Version: 35146-02/2018-05-04

Synopsis

Study site:	ENT departement, Sahlgrenska University hospital
Investigation code:	C58
Principal investigators:	Måns Eeg Olofsson, MD Phd [redacted]
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Sponsor:	Oticon Medical AB Datavägen 37 B 436 32 Askim Sweden
Monitor:	Oticon Medical representatives
Objective(s):	The primary objective of this study is to validate the performance of the externally worn sound processor named the Fusion sound processor (SP). In addition the study will evaluate magnet strength head, potential skin problems and retention in daily life. Focus will also be on user satisfaction, usability and performance compared to current SP.
Methodology:	Prospective case study. 6-10 patients will be fitted with Oticon Medical Fusion SP
Product:	Fusion SP developed by Oticon Medical AB (Askim, Sweden).
Main inclusion/exclusion criteria:	Inclusion criteria • Subject implanted with BCI implant and using the BCI sound processor, [redacted] Exclusion criteria • Inability to participate in follow-ups
Intervention(s):	Fitting and evaluation of a sound processor to patient in daily life. Laboratory testing including speech in noise and aided thresholds measurements.
Duration of study period:	7 months
Criteria for safety:	No complications is anticipated. Serious adverse events and adverse events will be monitored thorughout the study.
Statistical methods:	Pairwise differences for continuous variables will be tested with Wilcoxon Signed Rank test and for ordered categorical variables with Sign test.
Investigation plan prepared by:	Marianne Philipsson, Clinical Trial Manager, MSc, Oticon Medical AB

Revision history:

Revision no	*Date*	*Description*
[redacted]	[redacted]	[redacted]

1. Contents

2. Appendix

A. Case report forms

3. Abbreviations

BAHS – Bone anchored hearing system
BBC – Bridge Bone Conductor
BC – Bone Conduction
BCI – Bone Conduction Implant
eCRF – electronic Case Report Form
dB – Decibel
IPS - Infection/Irritation, Pain, Skin height/numbness - scale
N/PA – Newton Pascal
PTA – Pure Tone Average
SNR – Signal to Noise Ratio
SP – Sound Processor
SPL – Sound Pressure Level

SRS – Speech Recognition Score
SSQ – Speech, Spatial and Qualities of hearing

4. Introduction

Bone conduction hearing systems use the body's natural ability to transfer sound through bone conduction. The sound processor picks up sound and converts it into vibrations that are transferred through the skull bone to the inner ear (cochlea). Thus, for patients with conductive or mixed hearing losses, patients with lasting hearing loss following a middle ear disease or malformations (such as microtia), the vibrations are bypassing the conductive problem in the ear canal or middle ear. For single sided deaf patients, one utilize that the vibrations are transmitted to the cochlea on the contralateral side. [3] Bone conduction devices currently on the market are divided into three types; transcutaneous direct drive, percutaneous (skin penetrating) direct drive and transcutaneous skin drive bone conduction devices. [redacted]

The primary objective off this study is to validate the performance of the externally worn sound processor named the Fusion SP. In addition the study will evaluate magnet strength head, potential skin problems and retention in daily life. Focus will also be on user satisfaction, usability and performance compared to current SP.

5. Background

Bone conduction hearing systems (BAHS) have been used since the late 1970th. More than 150.000 patients are using percutaneous BAHS world-wide [2]. Transcutaneous hearing systems are a further development of bone conduction hearing systems. They do not have a permanent skin penetration but use the same principle of bone conduction as BAHS as a mean to transfer the signal to the cochlea. In transcutaneous systems the sound is picked up by a microphone and the processed signal is transmitted through the intact skin to the implant. These kind of transcutaneous systems utilizes direct drive bone conduction, as does BAHS, and the vibrations are transferred to the skull by an implanted transducer [2]. See figure 1.

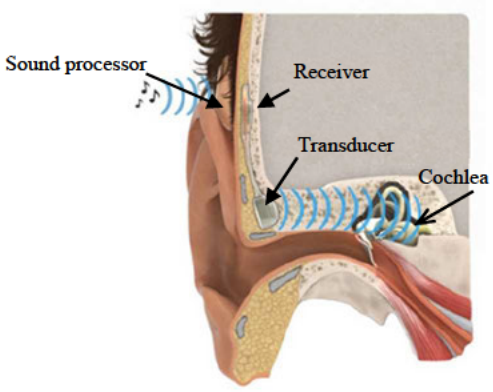

Figure 1 Transcutaneous direct drive bone conduction device

There is currently one transcutaneous bone conduction system in the market; Bonebridge (MedEl, Innsbruck Austria). Bonebridge has been available since 2012 and several studies have shown the Bonebridge to be safe [5-11] with good audiological performance in terms of improving hearing thresholds with on average 31dB ([5], [7], [9], [10], [12], [13], [14] and speech intelligibility [12], [15] Also subjective outcome in terms of both satisfaction [7], [11] and performance [8], [12] shows positive results. The literature shoes that transcutaneous is a well proven technology that benefits patients and it can only be expected that this technology will become more and more used within the field of bone anchored hearing.

Figure 2 The BCI system with the BCI SP and BCC Transcutaneous direct drive bone conduction device

replaced by the Oticon Medical Fusion SP.

6. Identification and description of the investigational device

The Fusion SP (see Figure 3) is, , intended for improvement of hearing for patients with conductive and mixed hearing losses by unilateral or bilateral fitting, as well as patients suffering from single sided deafness. The SP is worn on the side of the head and is daily placed attached and detached by patients themselves based on need and preference. The Fusion SP intends to pick up the sound and convert to an electric signal that is processed to fit the patients hearing loss and specific needs though signal processing algorithms programmed to the SP's digital chip. The signal is then converted to an electric magnetic signal transmitted from the transmitter coil in the SP to the receiver coil in the implant unit through the intact skin via a magnetic induction loop system. The Fusion SP includes a magnet, a microphone, battery, sound processing electronics and a radio frequency tuned switching power amplifier that drives the transmitter coil inductive link. The SP is placed above the implant which is located in the mastoid bone behind the ear, the SP is held in place by magnet forces and can easily be removed and reattached by the patient. All materials in contact is biocompatible [19]

Figure 3. The Fusion sound processor, to the left seen from the front and to the right seen from the side.

[redacted]

7. Justification for the design of the clinical study

[redacted]

[redacted]

[redacted]

[redacted] To be consistent with earlier research on transcutaneous system comparison will be made primarily compared to the unaided condition. But since the subjects already have a device, the BCI SP, comparisons will also be made to this device. The duration of the study, 6 months, has been chosen to allow the patients to acclimatize to the new SP as well as give a relevant time for evaluation of skin reactions and magnet retention forces. In addition a 7th month is added to the study to allow evalution of a new optimized setting.

8. Risks and benefits of the investigational device and clinical evaluation

A risk analysis have been performed according to ISO 14972 showing that the benefits of the Fusion sound processor outweigh the residual risks [16]. It can be concluded that since the study only aims at fitting a new sound processor on already implanted subjects the risk of participating in the study is low and comparable to any SP change or upgrade within clinical practice [redacted] This will require an extra effort for the subjects, however generally the possibility to optimize ones sound experience is seen as something positive for people with hearing impairment. The subjects will get access to a new SP with the latest technology and will have the opportunity to interact with the experts within the field of bone anchored hearing systems. The continued development of sound processors compatible with the subjects' implanted system will grant the subjects access to continuous use of the system.

We conclude that the risk of participation in this clinical study is minimal. The additional effort required of the participating subjects is deemed acceptable when weighted against the subject's expected benefit in terms of trying a new sound processor with the latest technology and increasing the subject's options of available hearing devices. This study will also provide input to the development of, and help bring, a new bone conduction hearing device to market, which will provide the hearing impaired population with an additional treatment option.

9. Objectives and hypotheses

9.1. Primary Objective and hypothesis

- The primary objective off this study is to validate the performance of the Fusion SP. Performance will be investigated in terms of improvement of aided sound field thresholds with the Fusion SP compared to the unaided condition. The hypothesis is that there will be a significant improvement in aided thresholds with the Fusion SP compared to unaided.

9.2. Secondary Objectives and hypotheses

- Magnet strength measured on the subjects' head and potential skin problems when wearing the Fusion SP, where the hypothesis is that wearing the SP with the magnetic attachment to the skull will not cause any problem with adverse skin reactions.
- Retention in daily life, where the hypothesis is that the Fusion SP can sustain the forces caused by daily movement eg. walking, walking up and down a stair and jogging. Extensive movement such as heavy exercising or physical work will require an extra holding option such as a safety line attached to the SP.
- Speech intelligibility performance compared to unaided. The hypothesize is a significant improvement for the Fusion SP compared to without SP.
- User satisfaction and usability focusing on evaluation and optimizing technical features. Our hypothesis is that satisfaction with the Fusion SP is as good as or better compared to the current solution.
- [redacted]
- Subjective evaluation of appearance of the SP, absolute and compared to their current SP as cosmetics is of great importance to users. We hypothesize that the appearance of the Fusion SP will be experienced as positive.

9.3. Tertiary Objective

An additional objective of this study is also to use measurements from the fitting visit to increase our knowledge and to provide input to further development of transcutaneous solutions.

- BC in-situ measurements. The BC in-situ measurement is made as a part of the fitting where the hearing thresholds are measured through the SP.
- [redacted]

10. Design of the clinical investigation

The study is a seven months prospective study on subjects implanted with the BBC device and using the BCI SP.

The subjects will be followed for seven months to ensure that an adequate monitoring of the skin condition can be made and that the subjects have been completely acclimatized to the sound of the Fusion SP and also allow for evaluation of an additional setting. [redacted]

Audiological measurements on the Fusion SP will be made at visit 2 and visit 3 to be able to track which impact of fine tuning the instrument have and on visit 4 to measure when subjects have been fully acclimatized to the sound of the Fusion SP. The audiological measurements on the BCI SP will be carried out at visit 2 when the subjects still are fully adapted to the BCI SP to test the comparator under the most favorable condition. In addition audiological measurements off an additional setting will be carried out on visit 5 to be compared to the measurments performed on visit 4 as well to the BCI.

During the test period of seven months, the Fusion SP will be used by the subject instead of the BCI SP to investigate the subjects' experience and satisfaction with the Fusion SP compared to the previously worn BCI SP. Their subjective experience using the Fusion SP will be gathered through questionnaires where focus is on the individual's experience of the sound including parameters such as sound quality, listening comfort, loudness and speech intelligibility. There will also be questions concerning usability and appearance of the device.

The retention of the device will be evaluated through questions aiming at tracking different activities and activity levels by the subjects together with potential SP falling off the heads and subjects worrying about loosing the sound processor. These answers will also be held up against the magnetic force measurements tracking subjective evaluation of SP falling of, i.e. activity levels to actual magnetic retention forces.

[redacted]

Adverse events and serious adverse events will monitored throughout the study visits.

10.1. Endpoints

10.1.1. Primary endpoints

- Primary endpoint of this study will the difference between Fusion-aided and unaided sound field Pure Tone Average of thresholds at frequencies 500, 1000, 2000 and 4000 Hz (PTA 4) after six month use of the processor.

10.1.2. Secondary endpoints

- Difference between Fusion-aided and unaided sound field Pure Tone Average of thresholds at frequencies 500, 1000, 2000 and 4000 Hz (PTA 4) after seven months use of the processor.

- Difference between Fusion-aided and unaided sound field Pure Tone thresholds at frequencies 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz after six months use of the processor.

- Difference between Fusion-aided and unaided sound field Pure Tone thresholds at frequencies 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz after seven months use of the processor.

- Difference between Fusion-aided sound field PTA 4 at
    - 6 months and 1 months
    - 6 months and 0 months
    - 1 months and 0 months
    - 6 months and 7 months use of the sound processor

- Difference between Fusion-aided sound field pure tones at frequencies 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz at
    - 6 months and 1 months
    - 6 months and 0 months
    - 1 months and 0 months
    - 6 months and 7 months use of the sound processor

- Difference between Fusion-aided after 6 month of use and BCI-aided sound field PTA 4.
- Difference between Fusion-aided 7 months of use and BCI-aided aided sound field PTA 4.

- Difference between Fusion-aided after 6 month of use and BCI-aided sound field pure tones at frequencies 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz
- Difference between Fusion-aided 7 months of use and BCI-aided sound field pure tones at frequencies 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz

- Difference between Fusion-aided and unaided speech intelligibility scores (in % correct) after six month use of the processor.
- Difference between Fusion-aided and unaided speech intelligibility scores (in % correct) after seven month use of the processor.

- Difference between Fusion-aided and unaided sound field speech intelligibility scores in SNR after six months use of the processor.
- Difference between Fusion-aided and unaided sound field speech intelligibility scores in SNR after seven months use of the processor.

- Difference between Fusion-aided speech intelligibility scores (in % correct)
    - at 6 months and 1 months
    - 6 months and 0 months
    - 1 months and 0 months
    - 6 months and 7 months use of the sound processor

- Difference between Fusion-aided sound field sound field speech intelligibility scores in SNR
    - at 6 months and 1 months
    - 6 months and 0 months
    - 1 months and 0 months
    - 6 months and 7 months use of the sound processor

- Difference between Fusion-aided after 6 month of use and BCI-aided speech intelligibility scores (in % correct)
- Difference between Fusion-aided 7 months of use and BCI-aided sound speech intelligibility scores (in % correct)
- Difference between Fusion-aided after 6 month of use and BCI-aided sound field speech intelligibility scores in SNR
- Difference between Fusion-aided 7 months of use and BCI-aided sound speech intelligibility scores in SNR

- Difference in magnet strength measured on the patient's heads in Newton
    - after 6 and 1 months
    - after 6 and 0 months
    - after 1 and 0 months
    - after 6 and 7 months use of the sound processor.

- IPS (Infection/Irritation, Pain, Skin height/numbness - scale) score at baseline, one, six and seven months use of the sound processor.
- Retention in daily life after one and six months of use as measured by questionnaire
- User satisfaction and usability evaluation as measured by questionnaires after 1, 6 and 7 months of use.
- Subjective performance as measured by SSQ (BCI at fitting, Fusion 1 & 6 months)
- Difference in performance as measured by SSQ between Fusion-aided after 6 month of use and BCI-aided

10.1.3. Tertiary endpoints

- BC-insitu hearing thresholds for frequencies 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz
- Unmasked BC-insitu on implanted ear for frequencies 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000 and 8000 Hz
- Gain curves evaluating feedback limits in dB N/Pa

[redacted]

10.2. Outcome measures

10.2.1. Test subject characteristics

We will collect the following subject characteristics (please refer to Form 1 in Appendix A for details).

- Gender
- Age

- Hearing thresholds
- Hearing device history
- Medical history related to BBC implant

10.2.2. Primary outcome measures

- Aided and unaided sound field threshold measurements

10.2.3. Secondary outcome measures

- IPS score
- Picture of skin condition
- Questionnaires
  - Speech, Spatial and Quality of hearing (SSQ) [18]
  - Questionnaire developed by Oticon Medical about:
    - Usability and satisfaction using the Fusion sound processor
    - Activity and activity levels together with risk of the SP to fall off developed by Oticon Medical

    The questionnaires come in different versions focusing on relative measures.
  - User diary developed by Oticon Medical with specific situations specified for the subjects to seek out and evaluate the SP in.

- Sound field speech intelligibility measurements
  - Signal to noise ratio (Hagerman). Speech level kept constant at an average level of 63 dB SPL.
  - Speech recognition score in noise (SRS) using monosyllabic words (SNR=4 dB).
- Pictures of the SP on the subject's head
- Magnet strength measurements

10.2.1. Teritiary outcome measures

Measurements carried out on the Fusion sound processor during the fitting

- BC in-situ measurement. Threshold measurement via the Fusion SP.
- BC threshold measurement. Conventional audiometric measurement
- Feedback margin measurement. Gain measurement via the Fusion SP.
- [redacted]

Follow-up visits	*Screening* *contact by phone*	*Visit 1* *Baseline*	*Visit 2* *Fitting visit*	*Phone call* *1 -2 week after visit 1*	*Extra visit* *(optional)*	*Visit 3* *Follow up 1 month*	*Visit 4* *Follow up 6 month*	*Visit 5* *Follow up 7 month additional setting*	*Unscheduled visit*
Information	***X***	***X***					***X***		
Subject characteristics		***X***							
Skin evaluation		***X***			***X***	***X***	***X***		***(X)***

Signing informed consent		*X*					*X*		
BC-thresholds			*X*						
Interview about SP				*X*		*X*	*X*	*X*	*(X)*
Fitting of sound processor			*X*						
BC In-situ			*X*						
Feedback margin measurement			*X*						
Fine tuning			*(X)*		*X*	*(X)*	*X*	*(X)*	*(X)*
[redacted]			*(X)*		*(X)*	*(X)*	*(X)*		*(X)*
Skull simulator			*X*		*X*	*(X)*	*X*		*(X)*
Magnet retention force			*X*			*X*	*X*		*(X)*
Sound field threshold and speech			*x BCI x Fusion*			*x Fusion*	*x Fusion x Unaided*	*X Fusion new setting*	
AE				*X*	*X*	*X*	*X*	*X*	*X*
Questionnaires			*x BCI*			*x Fusion*	*x Fusion*	*X Fusion new*	
Photo			*X With SP*			*x Without SP*	*x Without SP*		*(X)*

Table 1 Content of Fusion sound processor study

10.3. Investigation outline

Screening

[redacted]

The subjects will be contacted by phone by the sub-investigator who is well-known to the patients. The subject will be thoroughly informed about the study purpose and content including all study related visits. If the subject initially on the phone shows interest in participating in the study, informed consent together with written information will be sent to the patient and a first visit will be booked with the investigator.

First visit:

- Go through patient information and sign informed consent
- Patient's demographical data is registered in the electronic Case Report Form
- Skin evaluation

At the first visit the patient information will be gone through together with the subject and the patient will have the possibility to ask questions on the study and study procedures. If the subject wishes to participate in the study, the informed consent is signed. The investigator will then perform a base line skin evaluation.

Second visit, Fitting:

- Fill out the questionnaire for BCI SP
- Perform conventional BC-threshold measurements through audiometer and BC71 vibrator.
- Fitting of the Fusion sound processor including BC-insitu and feedback manager.
- Skull simulator measurements on the Fusion SP and BCI SP
- Sound field thresholds and speech intelligibility measurements on the BCI SP and Fusion SP
- Magnet force measurement
- Photo of the sound processor on the head
- Hand out of questionnaires for evaluation of Fusion SP
- [redacted]

The subject will start by filling out the questionnaire to evaluate the BCI SP. After that the fitting of the Fusion SP will be performed, a part of the fitting is to measure BC-insitu and feedback manager. As a reference for the BC- insitu thresholds conventional audiometric BC thresholds will also be measured at the second visit. The subjects' initial opinion about the sound will indicate if there is a need for fine tuning or not. The subject will be given the possibility to walk around with the SP in place and evaluate the sound.

Sound field thresholds and speech intelligibility measurements will be performed both on Fusion SP and on BCI SP and photos will be taken with the sound processor on the head. To check the retention force of the magnet a magnet force measurement will be performed together with an evaluation of magnet strength and potential shift of magnet to a stronger or weaker if deemed necessary by the sub-investigator. At last questionnaires used for Fusion SP evaluation will be handed out.

[redacted]

If convenient for the subject, visit 1 and visit 2 can be carried out at the same day.

Phone call and potential extra visit

- Adverse events during the test period
- Evaluate need for fine tuning and conduct fine tuning
- Skull simulator on Fusion SP after fine tuning
- [redacted]

After approximately one week of usage the test subjects will be contacted by phone and interviewed about the usage of the Fusion SP. The purpose with the phone call is to in an early stage address potential issues using the Fusion SP as the setting potentially could differ somewhat compared to what the test subjects have been used to. If deviations are judged to be severe and affect the usage of the SP the test subject will be offered to come in for an additional fine tuning. At the extra visit fine tuning of the Fusion SP will be performed. The fine tuning will be verified through skull simulator measurements.

Third visit, one month after fitting:

- Adverse events during the test period

- Hand in questionnaire and interview about sound processor
- Magnet force measurement and skin evaluation
- Fine tuning if needed
- If fine tuning: skull simulator measurement with Fusion SP after fine tuning
- Sound field thresholds and speech intelligibility measurements Fusion SP and unaided
- Photo of the area under the sound processor.
- Hand out of questionnaires for evaluation of Fusion SP
- [redacted]

At the third visit after one month the test subjects hand in questionnaires on Fusion SP and magnet forces are measured again. Sound field thresholds and speech intelligibility measurements on Fusion will be performed. A photo of the area under the SP will be taken to help with evaluation of skin condition. If needed fine tuning will be performed with skull simulator measurement after. In the beginning of the visit eventual adverse events during the test period will be noted.

Fourth visit, six months

- Adverse events during the test period
- Hand in questionnaires
- Magnet force measurement and skin evaluation
- Sound field thresholds and speech intelligibility measurements on Fusion SP
- Fine tuning to apply additional setting
- Skull simulator on Fusion SP after fine tuning
- Adverse events during the visit.
- [redacted]
- Go through information about adding on an extra visit
- Signing informed consent for adding an extra visit

Fifth visit, seven months

- Adverse events during the test period
- Hand in questionnaires
- Sound field thresholds and speech intelligibility measurements on Fusion SP
- [redacted]
- If finetuning: Skullsimulator simulator on Fusion SP after fine tuning

On the fourth visit the magnet force measurements and pictures of the skin under the SP will be repeated. Sound field thresholds and speech intelligibility measurements will be conducted, this time for the Fusion SP and unaided. There is also a possibility for extra fine tuning if needed. In the beginning of the visit adverse events during the test period will be noted.

Unscheduled visits

If any problems arise under the trial, the subjects are advised to contact the sub-investigator. The sub-investigator will evaluate and confer with the investigator if needed. If the problems are SP related (eg. need for fine tuning, loss of SP or malfunctioning SP) appointment with the sub-investigator or if of medical character (eg. skin problem or pain the area under the SP) refer to investigator who will schedule an extra visit.

10.4. Investigational device and comparator

The investigational device is described in Sec. 6. Exposure time of the investigational device is expected to be somewhere from a minimum of 5 hours up to a full day's use, 16 hours. The usage is expected to be the same as the usage of patient's current device, the BCI SP.

10.4.1. Comparator

The study primary objective is comparing the investigational device to the unaided condition. The subjects included in the study will all have been implanted with the BCI implant and are using the BCI SP. For secondary objectives only, the BCI SP will thus be the comparator device in the study. Just as in the Fusion SP, the sound is picked up, processed and transmitted from a transmitter coil through the intact skin to a receiver coil in the BC unit via a magnetic induction loop system. Both the Fusion and BCI SP has possibility for volume change and several programs with different settings based on user preference.

[redacted]

10.5. Subject population

All BCI subjects that are included in and have worn the BCI sound processor for one year in the Osseofon study will be offered to participate in this study according to the inclusion criteria below. At the time of enrolment, 13 subjects fit this criteria making up the eligible population for this study. We expect between 6-10 of the subjects offered to participate will accept and be enrolled. The current Osseofon study have no drop outs [17] and we therefore expect all the subjects to fulfil the study and that there is no drop outs during the course of the study. The total time a patient will be enrolled in this study is six months.

[redacted]

Inclusion criteria

- Subjects implanted with the BBC implant
- [redacted]
- [redacted]
- Active user of the BCI SP

Exclusion criteria

- Inability to participate in follow-ups
- Unsuitable as judged by the principle investigator or the sub-investigator

10.5.1. Sample size calculation

The sample size calculation is based on the primary end-point. With Wilcoxon Rank test (compare Sec. 15. Statistical considerations) we need a minimum of 6 patients to reach statistical significance if all show improvements. Results from the BCI study on 6 patients [21] and studies on Bonebridge (another transcutaneous system with similar intended use and population, please refer to Sec. 5) show an average difference between aided and unaided free-field thresholds of 31dB (Sec. 5). Based on knowledge in the field and the primary end-point of this study, the minimum sample size is therefore 6 patients.

This sample size, although limited, will also provide valuable data on more general performance and satisfaction with the device, as described in the secondary objectives of the study. We therefore conclude that the minimum of six included patients is an adequate sample size.

11. Study Procedures

11.1. Fitting

[redacted]

11.2. Measurements

11.2.1. Magnet force measurement

To measure the pull off force in Newton a digital force gauge will be used together with a measuring adaptor with a magnet corresponding to the magnet in the SP. Both axial and parallel forces will be measured. For parallel force the force gauge is pulled straight up while the patient sits with the head straight. For axial forces, the force gauge is pulled straight up while the patient tiles the head to the side.

11.2.1. Skull simulator measurement

To measure the output of the Fusion sound processor a skull simulator is used. The skull simulator simulates the mechanical impedance of the head when a bone anchored sound processor is attached to it.

[redacted]

11.3. Clinical assessments

11.3.1.1. Photo

Photos should be taken of the Fusion SP on the test subject's head from a 0° and 90° angle with the sound processor on and from 90° without the SP on to assess the physical appearance and fit of the device together with the potential skin reactions. The pictures will be taken with the SP or the area under the SP in center and without being able to identify the subject.

11.3.1.2. BC-thresholds

Detection of thresholds through audiometer and using a BC71 vibrator as used for measuring conventional audiometry. Pure tone signal at 250 Hz, 500Hz, 750Hz, 1kHz, 1.5kHz, 2 kHz, 3kHz, 4kHz, 6kHz, 8kHz.

11.3.1.3. Aided Sound field thresholds

Detection thresholds with/without BAHS. Warble tone signal presentation via loudspeaker. 250 Hz, 500Hz, 750Hz, 1kHz, 1.5kHz, 2 kHz, 3kHz, 4kHz, 6kHz, 8kHz

11.3.2. Speech to noise thresholds (Hagerman).

Speech recognition test using five word matrix sentences. The material is based on a list of ten spoken Swedish sentences computer edited to obtain new lists with exactly the same words but put together into new sentences [1]. Speech level kept constant at an average level of 63 dB SPL and noise adapts to find the signal to noise ratio where the test subject repeats 50% of the words correct. The order of testing the BCI SP and Fusion SP on visit 1 and Fusion SP and Unaided on visit 2 will be altered not favor any of the conditions due to either learning or fatigue effects. Also the speech list used for testing will be balanced avoiding the same list to be used too many times.

11.3.3. Speech recognition score in noise (SRS) using monosyllabic words

A list of 50 Swedish monosyllabic words is presented to the patient at a level of 68 dB SPL with a constant speech shaped noise present. The signal to noise ratio is 4 dB and the number correct words in percent is obtained. The order of testing the BCI SP and Fusion SP on visit 1 and Fusion SP and Unaided on visit 2 will be altered not favor any of the conditions due to either learning or fatigue effects. Also the speech list used for testing will be balanced avoiding the same list to be used too many times.

11.3.4. Skin assement evaluation

Used for skin assessment is the recently developed IPS scale consisting of three parts: I (Infection/Irritation-scale) ranging from 0-4, P (Pain-Scale) ranging from 0-2 and S (Skin height/numbness-scale) ranging from 0-2. A higher score on either of the subscales reflects a more severe complication [20].

12. Monitoring plan

During the investigation, representatives from Oticon Medical will have regular contact with the investigation site. According to Good Clinical Practice (GCP) guidelines, the main task of the clinical trial monitor is to oversee the progress of a clinical study and to ensure that:

- The rights and well-being of human subjects are protected
- Reported trial data are accurate, complete and verifiable from source documents
- The conduct of the trial is in compliance with the currently approved protocol, SOPs, GCP and applicable regulatory requirements

Authorized representatives of the sponsor will therefore visit the centre to perform inspections as well as monitor the data captured in the electronic data system throughout the study.

13. Investigation administrative structure

[redacted]

13.1. Information to be supplied to the clinical investigator

Before initiating the clinical investigation, the principal investigator and sub investigator will receive all written study and device related information.

13.2. The patient's medical record

The subjects's participation in the clinical investigation will be documented in the patient's medical record along with test subject code, title of the investigation and investigation code. This will be done

by the investigator at the first visit. It will also be documented that the patient has been informed about the study and that the patient has signed the informed consent form. The date of inclusion into the study will be recorded together with the study code. When leaving the study that date will be recorded. Note that if AEs warrants follow-up the date that the last activity to follow the AE up is the last date in the study and not the last visit date. The last date of AE follow-up may have the status ongoing, not recovered or unknown. Ongoing will be used only when a status quo have been reached. Unknown may be used when the subject has been lost to follow-up.

13.3. Data handling

All data concerning trial subjects is protected under the Personal Data Act (Personuppgiftslagen (1998:204)) and the Health and Medical Service Act (Hälso- och sjukvårds lagen) and will be handled accordingly. After 25 May 2018 the data for the trial subjects is protected under the General Data Protection Regulation (GDPR)All information about the subjects is under professional secrecy. All information about the subjects outside the clinic will be anonymized and the subjects identity will not be known for anyone outside the clinic.

The sub-investigator will, during the study, hold the appointments with the subjects at an external location outside the hospital at Chalmers Technical University where the appropriate measurement facility is located. No personnel from Chalmers will be involved in the study visits besides acting as technical support for the measurement facilities. No patient data will be shared with the personnel and they will get no access to any information about the patient.

13.4 Suspension or premature termination of the clinical investigation

If the investigation is terminated prematurely or suspended, the sponsor will promptly inform the clinical investigation centre of the termination or suspension and the reason(s) for this. The competent authorities and the ethical committee will also be informed promptly in writing and provided with the reason(s) for the termination or suspension by the sponsor. The sponsor may at any time terminate the clinical investigation due to circumstances related to the product or company that preclude ongoing patient treatment.

14. Data management

Data captured will be recorded in the electronic Case Report Forms (eCRF). In appendix A the content of the eCRFs are specified. All data, subject and product related, must be accurately recorded in the eCRF by the investigator and/or delegated site staff, in this case the sub-investigator All patient related questionnaires will be filled out anonymously and will only be identified by the subject code. The patient code on all questionnaries and CRFs will ensure tracebility of data. All data gathered by questionnaire will be added in the eCRF by the sub-investigator.

All users of the eCRF system have personal, password protected accounts allowing tracking of all data entry in the system. Data management and data cleaning will be continuously performed in the eCRF using the queries function to ensure traceability of all data entry and changes by the assigned data manager. Data management is performed by the Sponsor. Monitoring will be performed against source data in patient journals. The monitor will have access to the subject's identity and will sign an agreement in accordance with the hospital practice to ensure patient confidentiality. All subjects will be given a code that will make the subject's identity unknown to external parties such as the sponsor.

It is the responsibility of the investigator to make sure that subject identification listings with subject code and identity are kept. These lists, source data and a copy of the eCRF data shall be retained for 5 years after the study has been completed.

14.1.1. Data management procedures

Database lock will be agreed by data manager, principal and sub investigator, and study project leader in a clean file meeting before any data analysis. Database lock will be done at the end of the study, when all six month data is available.

14.2. Confidentiality

At all times throughout the clinical investigation confidentiality will be observed by all parties involved. All data will be secured against unauthorized access.

15. Statistical considerations

To evaluate the differences between the unaided and Fusion SP aided threshold at 6 months (primary end-point) a non-parametric test (Wilcoxon Signed Rank test) will be used.
A detailed statistical analysis plan (SAP) will developed prior to database lock by an independent bio-statistician (compare Sec. 13). In general, pairwise differences for continuous variables will be tested with Wilcoxon Signed Rank test and for ordered categorical variables with Sign test. Last value carried forward will be used for potential drop-out subjects. If imputation is used, sensitivity analysis will be performed for the primary outcome, and selected additional outcome variables as defined in the statistical analysis plan.

16. Amendments to the CIP

In case of changes to the clinical trial protocol are needed, an amendment should be made. Substantial amendments should be approved by the competent authorities and ethical committee before incorporated.

17. Deviations from clinical investigation plan

The investigator should not deviate from the clinical investigational plan except if needed to protect the rights, safety and well-being of the subjects. Such cases such be documented and reported to the EC and the Sponsor as soon as possible.

If deviations (other than mentioned above) occur, the Investigator should inform the monitor/clinical study manager and recorded in the protocol deviation log provided in the study site file. The implications of the deviation must be reviewed and discussed between the Sponsor and the Investigator. If deviations are found during monitoring visits, they should also be documented in the monitoring report and handled as above. This should be done as soon as possible after detection to avoid repetitive deviations. Continuous review of protocol deviations during monitoring visits aim to detect systematic errors and to identify retraining needs at the site. Frequency of monitoring is described in the monitoring plan and should be increased if systemic deviations are identified.
All protocol deviations must be documented stating the reason, date, the action(s) taken, and the impact for the subjects and/or the study.
If serious or repeated deviations occurs, the Sponsor has the right to initiate early termination of the study.

At the end of the study, protocol deviations will be categorized as minor or major and their consequence on analysis populations will be decided.

18. Device Accountability

Each device prepared for the clinical study will get a unique serial number that will be marked on the device and on the box of the device. The devices will be brought by sponsor representative for each of the fittings as the sponsor responsible also will assist with the fitting. The device serial number will

be noted in the eCRF at the fitting visit. The sponsor will also keep a log of the device number and subject number. If any SPs are exchanged during the study the new number will be noted down together with date of exchanging the SP.

19. Statements of compliance

The clinical investigation will not be commenced until approval from both applicable regulatory authority and ethical committee has been received.

Ethical conduct of the investigation
The clinical investigation will be performed in consistency with the current version of the Declaration of Helsinki (Washington 2002), ISO 14155-2011 and applicable regulatory requirements and any additional requirements imposed by the EC.

Regulatory authorities
The clinical study will be submitted to and approved, in writing, by the Swedish regulatory authorities (MPA) prior to commencing the study. Any substantial changes to the investigational plan will be submitted for review. In case of any serious adverse events (SAE) the regulatory authority will be informed.

Ethics review
The investigation plan, including the final version of the patient Information and Consent Form must be approved in writing by an Independent Ethics Committee (IEC) before enrolment of any subject into the investigation. Substantial amendments to the Clinical Investigation Plan must be approved by the IEC if they influence the risk for the subject. Non-substantial amendments will be notified to the ethics committee.

Insurance
The subjects are covered by The Swedish Pharmaceutical Insurance and the Patient Injury Act. In addition the subjects are covered by insurance from the sponsor covering the use of the Fusion sound processor. This insurance covers use of the Fusion sound processor both during enrolment in this study but also use after study completion.

20. Informed consent process

The clinical investigator will ensure that the subject is given full and adequate oral and written information about the nature, purpose, possible risks and benefits involved. In this study this will be given over the telephone but also in written sent home to the subject. Subject will be notified that they are free to discontinue participation in the investigation at any time. The subject will be given time for consideration and the opportunity to ask questions before signing the informed consent form. This can be done by the subject contacting the investigator prior to the study or time will also be set aside on the first visit as the first thing on the visit. The subject signed informed consent must be obtained before conducting any procedures specifically for the investigation.

If any new information becomes available during the course of the trial that could influence the subjects' willingness to participate, the subject will be informed and asked to sign a revised informed consent.

The subject will consent in writing that the results obtained in the investigation may be used in authority assessment or submissions for publications in scientific journals with the condition that privacy and confidentiality is preserved. Subject will also consent in writing that concerned

personnel, sponsor representatives and concerned authorities may have access to the subject's medical record to perform source data verification.

The signed original of the consent form must be filed by the clinical investigator. A copy of the patient Information including the signed consent form should be given to the subject.

21. Adverse events, adverse device effects and device deficiencies

Any adverse events or serious adverse events, as described in Sec. 21.1 and Sec. 21.2, will be reported in this study as well as the parallel Osseofon study [redacted]. Any ongoing (S)AE at the conclusion of this study will be resolved in the Osseofon study. Any new AE's or SAE's that occur after the conclusion of this study but within the frame of the Osseofon study will be reported in the Osseofon study. An agreement to share relevant safety reporting data has been reached between the sponsors of the two studies to ensure adequate safety follow-up of the device.

21.1. Adverse Event (AE)

Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons whether or not related to the investigational medical device.

NOTE 1: This definition includes events related to the investigational device or the comparator.
NOTE 2: This definition includes events related to the procedures involved.
NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices.

21.2. Serious Adverse Event (SAE)

Adverse event that:

a) led to a death, injury or permanent impairment to a body structure or a body function.
b) led to a serious deterioration in health of the subject, that either resulted in:
- a life-threatening illness or injury, or
- a permanent impairment of a body structure or a body function, or
- in-patient hospitalization or prolongation of existing hospitalization, or
- in medical or surgical intervention to prevent life threatening illness
c) led to foetal distress, foetal death or a congenital abnormality or birth defect.

NOTE 1: Planned hospitalization for pre-existing condition, or a procedure required by the Clinical Investigation Plan, without a serious deterioration in health, is not considered a serious adverse event.

21.3. Device deficiency

Inadequacy of an investigational medical device related to its identity, quality, durability, reliability, safety or performance. This may include malfunctions, use error, or inadequacy in the information supplied by the manufacturer.

21.4. Adverse Device Effect (ADE)

Adverse event related to the use of an investigational medical device.

NOTE 1- This includes any adverse event resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the investigational medical device.

NOTE 2- This includes any event that is a result of a use error or intentional abnormal use of the investigational medical device.

21.5. Serious Adverse Device Effect (SADE)

Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

21.6. Unanticipated Serious Adverse Device Effect (USADE)

Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

NOTE: Anticipated SADE (ASADE): an effect which by its nature, incidence, severity or outcome has been previously identified in the risk analysis report 4.

21.7. Reportable Events

In accordance with the applicable regulatory guidelines and directives, the following events are considered reportable events;

- any SAE,
- any Device Deficiency that might have led to a SAE if:
  - a) suitable action had not been taken or
  - b) intervention had not been made or
  - c) if circumstances had been less fortunate
- new findings/updates in relation to already reported events.

21.8. Reporting Timelines

21.8.1. Report by sponsor to the National Competent Authority

Oticon Medical must report to the NCA (the Swedish MPA):

- all reportable events as described in 21.7 which indicate an imminent risk of death, serious injury, or serious illness and that requires prompt remedial action for other patients/subjects, users or other persons or a new finding to it: **immediately, but not later than 2 calendar days** after awareness by sponsor of a new reportable event or of new information in relation with an already reported event.
- any other reportable events as described in 21.7 or a new finding/update to it: **immediately, but not later than 7 calendar days** following the date of awareness by OM of the event.

21.8.2. Report by the investigator to the sponsor

Reportable events should be reported to Oticon Medical within 24 hours from when Investigator is first made aware of the event. Reporting to the ethical committee is done according to local regulation and is the responsibility of the Investigator.

22. Publication Policy

Prior to enrollment this study will be registered on ClinicalTrials.gov

When the primary clinical investigation is completed, even if prematurely terminated, a final report will be compiled.

[redacted]

23. Results and reports

When the clinical investigation is completed, even if prematurely terminated, a final report will be compiled. An interims analysis of the primary endpoint at 1 month will be compiled.
The results may also be used as basis for authority assessment. Privacy and confidentiality of information about each subject will be preserved in the report and any publication of the clinical investigation data.

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25. Signed agreements

25.1. Sponsor

On behalf of Oticon Medical AB I agree to the terms of this investigation plan.

Date and signature:

Name and title

25.2. Principal Investigator

I agree to the terms of this investigation plan. I will conduct the investigation according to the procedures specified herein and in consistency with the current version of the declaration of Helsinki and ICH Guideline for Good Clinical Practice (GCP).

Date and signature:

Name and title