Clinical Safety Investigation Plan/Protocol

Protocol Title:	**The iotaSOFT™ Insertion System Safety Study**
Investigational Product:	**iotaSOFT™ Insertion System**
Sponsor:	**iotaMotion, Inc.** **14 ½ S Clinton St** **Iowa City, IA 52240** **United States** **Phone:** **Fax:**
Document Number:	**iotaSOFT000001**
Version Number:	**1.0**
Date:	**February 19, 2020**
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Good Clinical Practices

This study will be conducted under Good Clinical Practices in accordance with US FDA, 21 CFR requirements for investigations of medical devices; in accordance with the Declaration of Helsinki; and in compliance with applicable Local and Federal Regulations.

Confidentiality Statement

This document contains confidential information of the Sponsor. This information is to be disclosed only to the recipient study staff and the Institutional Review Board or Institutional Ethics Committee reviewing this protocol. This information can be used for no other purpose than evaluation or conduct of this study without prior written consent from the Sponsor.

Investigator Signature

Protocol Title:	**The iotaSOFT™ Insertion System Safety Study**
Investigational Product:	iotaSOFT™ Insertion System
Protocol Number:	iotaSOFT000001v1

I confirm that I have read this protocol. I will comply with the protocol and the principles of Good Clinical Practice (GCP), as described in the United States Code of Federal Regulation (CFR) 21 Parts 50, 54, 56, and 812.

_____
Investigator Printed Name

_____ _____
Investigator Signature Date

1. SYSTEM OVERVIEW

1.1 The iotaSOFT™ Insertion System is an electrode array insertion tool that assists cochlear implant (CI) surgeons to insert CI electrode arrays with consistent insertion speed and force. The system consists of a single-use, sterile drive unit connected to a reusable, non-sterile touch screen control console and footpedal interface (Figures 1, 2, & 3. See also Overview Video 1 and Attachment 1 Device Description). After standard mastoidectomy and facial recess approach for cochlear implantation, the surgeon secures the stage base to the skull at superior edge of mastoidectomy with two pre-loaded self-drilling bone screws (Figure 3). The drive unit is placed into the stage base and the adjustable drive head is coupled to a compatible CI electrode. Using manual manipulation, the drive unit head is positioned outside the facial recess and aligned to the surgeon-desired electrode array insertion trajectory. Before insertion begins, the surgeon selects the desired speed from 0.1mm/sec to 1.0mm/sec in 0.1mm/sec intervals. With direct access and view of the surgical site, the surgeon controls the electrode insertion forward and reverse motion via footpedal while guiding the electrode array into the cochlea with standard CI instrumentation as necessary. Upon the completion of electrode array insertion and securing the array at the cochlea, the drive head and unit are uncoupled from the electrode lead and removed from the patient for disposal. The surgical site is closed and CI procedure is completed in the standard fashion.

Figure 1. Photos of (Left) iotaSOFT™ Insertion System – Controller and Accessories with computer console, power supply, rolling stand, footpedal, and extension cables coiled on stand basket. (Right) iotaSOFT™ Drive Unit and screwdriver in sterile packaging tray after Tyvek cover and sterile tray cover removed.

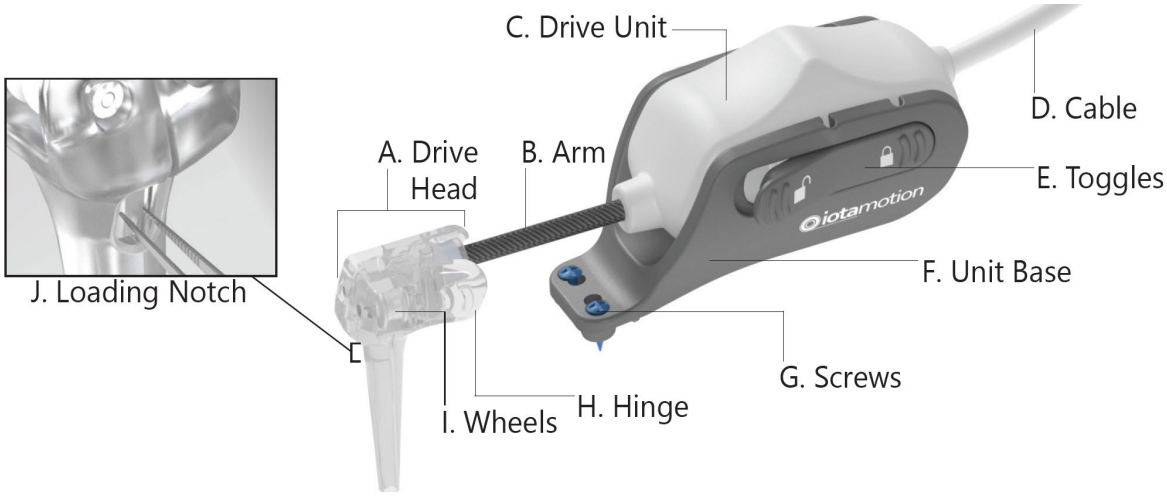

Figure 2. Representative rendering of iotaSOFT™ Drive Unit with parts labelled.

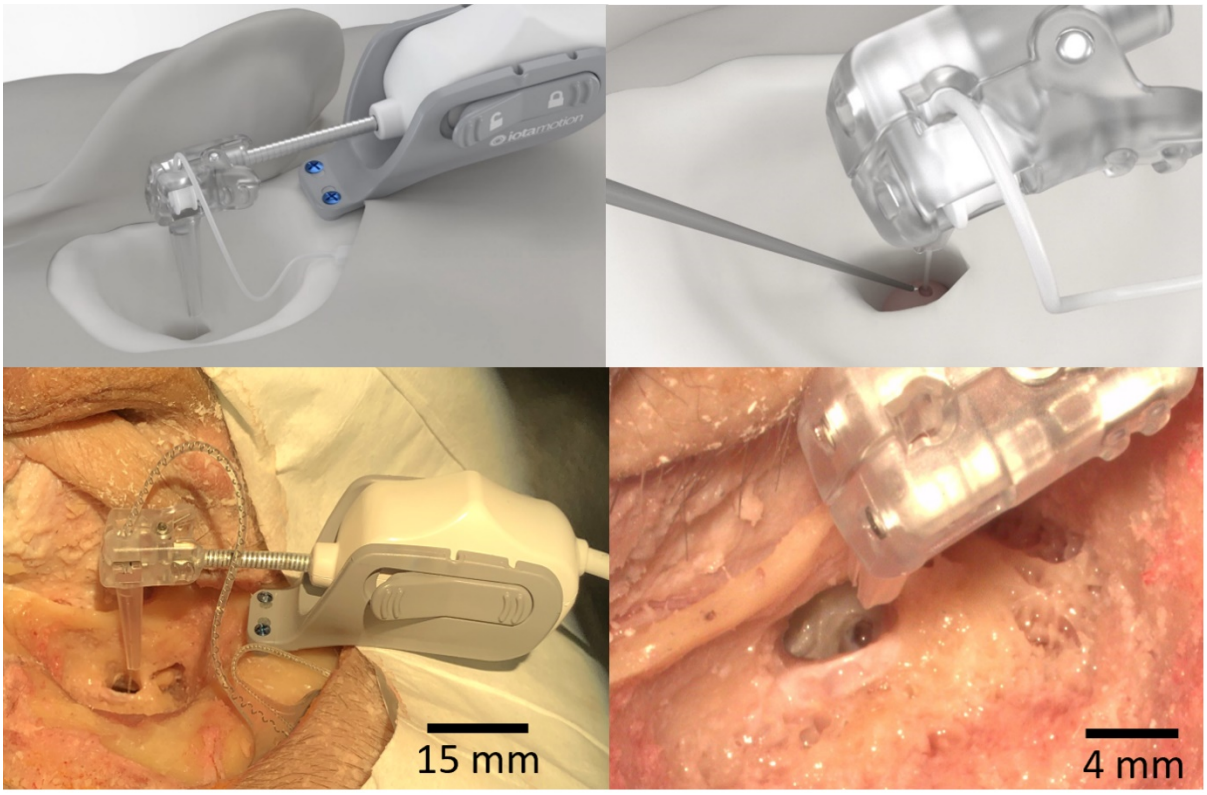

Figure 3. iotaSOFT™ Drive Unit at edge of mastoidectomy during insertion into cadaveric cephalus (bottom) and computer render (top). (Left) iotaSOFT™ Drive Unit secured at edge of mastoidectomy and electrode engaged in drive head outside the facial recess as intended during use. (Right) Closer view of surgical site showing view of round window is not inhibited by device when in position.

2. BACKGROUND

2.1 360 million people worldwide, or 5% of the global population, have disabling hearing loss (>40 dB). Moderate to severe hearing loss affects 6.3 million patients in the US, yet only 5-6% of people who meet CI candidacy criteria receive a CI.[1] The number of patients that could benefit from a CI is expected to dramatically rise which makes improving patient access to CI interventions of the utmost importance.

2.2. Since the first description of "atraumatic" insertion techniques in 1993,[2] numerous studies have shown that trauma to the cochlea during electrode insertion results in damage to delicate inner ear structures, reduced implant performance, and the potential loss of residual hearing.[3–7] While electrode array insertion technique has been shown to play a critical role in implant performance, the current standard of practice remains the use of manual forceps in which the inherent limitations of human kinematics makes slow and steady insertions difficult to achieve in a consistent manner.[8] Alternatively, there are dedicated implant-specific manual insertion tools which have limited to no ability to precisely control the insertion speed or insertion force variability. Therefore, there is a clear need for an insertion tool that performs slow and steady insertions for a more standardized and controlled technique.

2.3. Studies evaluating the effect of electrode array insertion speed on insertion forces have shown that greater speeds directly correlate with greater intracochlear forces.[9,10] Further, multiple studies demonstrate that high insertion forces damage the delicate structures of the cochlea, limiting CI performance and increasing the likelihood of the loss of residual hearing.[11–13] High insertion speeds have also been shown to increase the prevalence of intracochlear pressure spikes which can cause damage to the inner ear similar to loud noise exposure.[14–16]

2.4 Lastly, a clinical retrospective study evaluating CI recipients has shown that electrodes implanted at a "slow" manual speed (Average: 0.25mm/sec) experienced improved hearing preservation, decreased vestibular symptoms, and more complete electrode insertions compared to the "fast" speed (Average: 0.87 mm/sec).[viii]

3. INTENDED/INDICATIONS FOR USE

3.1 The iotaSOFT™ Cochlear Implant Electrode Insertion System is intended to aid the surgeon in placement of cochlear implant electrode arrays into a radiographically normal cochlea by controlling the speed of implant insertion.

4. BENEFIT

4.1 The benefit of the iotaSOFT™ Insertion System is to provide the surgeon a standardized, more controlled, and consistent method of inserting the electrode array compared to manual insertion techniques. The system enables the surgeon to perform CI electrode array insertions more consistently and slowly than the capabilities of human motion. Literature shows consistent and slow insertions decrease the risk of additional hearing loss or vestibular symptoms from inherently uncontrolled, variable, and excessively forceful manual insertions.[12] The iotaSOFT™ Insertion System also provides consistency of electrode array insertions among different ENT surgeons, helping to ensure that each patient receives an

equally slow and consistent insertion regardless of the surgeon performing the procedure or the electrode array used.

4.2. Known risks associated with manual cochlear implantation (the current gold standard) include electrode translocation, electrode tip fold-over, incorrect placement of electrode array, loss of residual hearing, and/or vestibular symptoms. Currently, experienced CI surgeons mitigate these risks by performing slow and steady atraumatic CI insertion techniques by hand. The iotaSOFT™ insertion system enhances the surgeon's ability beyond the capability of human motion during the electrode insertion and therefore has the potential to reduce the current risk profile inherent in the standard CI surgical procedure.

4.3. Similarly, by giving each ENT surgeon more confidence in their ability to insert electrode arrays with less variability during CI surgery, the system has the potential to expand patient access for those with severe hearing loss in which less than 5% of eligible patients receive a CI.

5.0 RISK

5.1. The risk profile of the iotaSOFT™ Insertion System is predicated on the fact that the vast majority of the CI implantation procedure remains unchanged from manual CI insertion techniques. Likewise, the critical risks associated with use of the iotaSOFT™ Insertion System are also associated with manual insertion, meaning the iotaSOFT™ Insertion System does not add critical risk to the surgical procedure. Use of the device also does not prevent a surgeon from stopping at any time and immediately reverting to manual insertion techniques, and therefore the risk to the patient does not exceed the current gold standard of care. Nonetheless, all risks related specifically to the iotaSOFT™ Insertion System have been reduced to the lowest probabilities ($<10^{-5}$) and have been mitigated by device design verification and validation by iotaMotion. A list of all potential patient risks, their severity, and the mitigation steps taken is outlined in Table 1.

Table 1. Potential patient risks and mitigation actions

Potential Risk (Harm)	Severity	Mitigation Completed
Device fragments in patient	Serious	Device Functional Testing
Electric shock not resulting in death	Critical	Electrical Safety Testing
Environment Harm (Limited) - simple contamination, localized effects of short duration	Minor	Labeling
Inconvenience or temporary discomfort. Customer dissatisfaction where there is no injury.	Negligible	Electrical Safety Testing Labeling
Irritation / inflammation of surgical site (permanent)	Critical	Biocompatibility Testing
Patient or user infection or cross infection (biosafety)	Critical	Sterilization Testing Packaging Validation Device Functional Testing Usability Study

Prolonged operative/ anesthesia time due to delay during surgery	Minor	Device Functional Testing Labeling Usability Study Electrical Safety Testing
Prolonged operative/ anesthesia time due to delay during set up	Negligible	Electrical Safety Testing Electromagnetic Compatibility Testing Labeling
Temporary discomfort	Negligible	Device Functional Testing
Unintended thermal tissue damage; no intervention required	Minor	Electrical Safety Testing Device Functional Testing

Severity Rating	
Catastrophic	Results in patient death
Critical	Results in permanent impairment or life-threatening injury
Serious	Results in injury or impairment requiring professional medical intervention
Minor	Results in temporary injury or impairment not requiring professional medical intervention
Negligible	Inconvenience or temporary discomfort

5.2. In addition to the testing listed as device-specific mitigations above, the device was evaluated against the current techniques to ensure no new risks (not listed above) were added by the use of the iotaSOFT™ Insertion System. The current known risks associated with manual cochlear implantation, including electrode translocation, electrode tip fold-over, incorrect placement of electrode array, loss of residual hearing, or vestibular symptoms, are currently attempted to be reduced by experienced CI surgeons performing slow and steady atraumatic CI insertion techniques by hand. The iotaSOFT™ insertion system enhances the surgeon's ability beyond the limits of human motion capabilities during CI insertions and therefore has the potential to reduce the current risk profile inherent in the standard CI surgical procedure. In summary, the risks associated with the iotaSOFT™ Insertion System have been successfully mitigated and are no worse than manual insertion. This conclusion was also supported by the results of the Cadaveric Comparative Analysis (see 6.1.3 Summary below and Attachment 4 for full report).

6 RISK MITIGATION – SUPPORTING DATA SUMMARY

6.1. As part of the overall risk mitigation, the iotaSOFT™ Insertion System was tested for functionality and safety in four categorical testing protocols and reports. Results are included in Attachments 2-5 and summarized briefly here.

6.1.1. Bench Performance Testing Report (Attachment 2 – Doc #720-036-0031)

This report verified the functionality of the system according to design inputs following simulated transportation and distribution and accelerated aging. The specific device requirements that were tested include:

6.1.1.1. The device performs to the desired speed (selected between 0.1mm/s and 1.0mm/s) within 20%.

6.1.1.2. The device can overcome electrode slip forces of at least 80mN.

6.1.1.3. The device has maximum insertion forces and insertion force variation significantly less than the literature derived manual insertion forces and force variation, <300mN and ≤400mN/sec respectively.

6.1.1.4. Forces imparted by the device during sheath removal following electrode insertion measured <100mN to ensure the device does not cause the electrode to dislodge during device removal.

6.1.1.5. Forces imparted by the device on the electrode measured significantly less than the maximum pinch force a surgeon could impart on the electrode using a pad pinch and forceps.

6.1.2. Benchtop Comparative Analysis Report (Attachment 3 – Doc #722-036-0021)

This engineering study compared the insertional force profiles obtained when inserting cochlear implant electrodes into synthetic cochleae using either manual technique or the iotaSOFT™ insertion system. Results showed that:

6.1.2.1. The average insertion force variation for iotaSOFT™ driven electrode arrays was 78% lower than the average insertion force for manually inserted electrodes at 0.1mm/sec and 70% lower at 1.0mm.sec. These comparisons were both significantly different ($p \leq 0.007$).

6.1.2.2. The average of maximum insertion force for iotaSOFT™ driven electrode arrays was significantly lower than average of maximum insertion force for manually driven electrodes ($p < 0.05$); for both insertion rates, a 51% and 32% reduction at 0.1mm/sec and 1.0mm/sec, respectively, was observed.

6.1.2.3. The iotaSOFT™ insertion system performed electrode array insertions with a lower variance of insertion force and force variation compared to manual surgeon insertions across surgeon skill levels. The total variance (cluster + residual) for the insertion force variation using the iotaSOFT™ assisted insertion was 186% and 190% lower than manual insertions for 0.1 and 1mm/sec respectively. Similarly, the maximum insertion force total variance for iotaSOFT™ assisted insertion was 190% and 188% lower compared to manual insertions across varying surgeon experience levels at both 0.1 and 1 mm/sec insertion rates, respectively.

6.1.3. Cadaveric Comparative Analysis Report (Attachment 4 – Doc #722-036-0020)

This report evaluated the effect of the iotaSOFT insertion system on the final intracochlear electrode array position and electrode functionality compared to manual insertion of cochlear implant electrode arrays in cadaveric cochleae during simulated operative use. Results showed that:

6.1.3.1. When compared directly to manual insertions, the iotaSOFT™ insertion system electrode insertions exhibited a lower percentage of intracochlear scala translocations, though the result was not statistically significant.

6.1.3.2. A lower percentage of tip fold-overs was also observed with the iotaSOFT™ insertion system electrode insertions when compared to manual electrode insertions, though this result was also not statistically significant.

6.1.3.3 A lower percentage of tip fold-overs was also observed with the iotaSOFT™ insertion system electrode insertions when compared to manual electrode insertions, though this result was also not statistically significant.

6.1.4. Usability Validation Report (Attachment 5 – Doc #712-036-0010)

The Usability Study assessed the occurrence of use errors related to the device. 16 ENT Surgeon/Nurse teams (in which the surgeons had completed a training session and training decay time) performed an CI implantation into a cadaveric cephalus in a simulated use environment. Test engineers observed insertions and noted any use errors, and user comments including a questionnaire and scoring table were collected. Results showed that:

6.1.4.1. Harms associated with the use errors found in the study were minor: prolonged operative/anesthesia time due to delay during surgery and prolonged operative/anesthesia time due to delay during set up. These minor potential harms were associated with use errors witnessed in a small percentage of users and tasks and were mitigated with a design change (eliminating the difficulties experienced with the device screwdriver) and updates to items emphasized in training. The residual use-related risk was minor and could not be further reduced with additional mitigations.

6.1.4.2. For all tasks, the use errors found could not lead to serious patient harm and no risk mitigations would lead to the reduction of overall or individual risks. The Usability results support that the iotaSOFT™ Insertion System is safe and effective for use by the intended users in a hospital setting. Surgeons can successfully use the iotaSOFT™ Insertion system to aid in placement of the electrode into the cochlea with nurse staff support.

7. CONCLUSION

The benefits of the device outweigh the minimal risks associated with the device. The iotaSOFT™ Insertion System provides the benefit of a 70% reduction in insertion force, 30% reduction in force variation (jerk), 180% reduction in variation between insertions with different surgeons or with different electrodes, and reduction in occurrence of electrode scala translocations and tip fold-over when compared to manual insertion. Furthermore, the iotaSOFT™ Insertion System is not statistically different than standard manual insertion techniques related to insertion angle, intracochlear scala position, and electrode electrical functionality. The risks associated with the device are not a significant clinical risk and are further mitigated by device completed design verification and validation testing as well as training provided to surgeons before the device can be used on patients.

8. STUDY PURPOSE AND ASSESSMENT

8.1 Study Purpose. The purpose of the proposed study is to evaluate safety of the iotaSOFT™ Insertion System when used by a surgeon to assist with inserting a cochlear implant electrode array. We will evaluate for successful device use during electrode array insertion via a surgeon questionnaire regarding device usability, monitor electrode array insertion time, assess CI electrode positioning or tip-fold-over by post-insertion X-ray, and measure electrode impedances and neural response telemetry at post-operative activation. A

set of relevant safety and effective use measures will be collected, and adverse events will be tracked and reported per applicable regulations.

8.2 Study Assessments

8.2.1 Surgeon Questionnaire

Surgeon questionnaires will be administered to solicit information about device utility, ease of device use during the procedure, and clinical workflow in the surgical setting. The surgeon questionnaire shall not contain any subject data and therefore, does not impact subject safety, welfare or confidentiality. The questionnaire will be completed by the implanting surgeon following completion of the surgical procedure. The information will be gathered and tabulated for qualitative analysis. For more details, see the surgical questionnaire (FRM00002).

8.2.2 Surgical Electrode Array Insertion Timing

iotaSOFT™ CI insertion system utilizes the same surgical approach and procedure as current manual CI insertion techniques without alteration to the approach workflow. The current standard CI surgical procedure includes a cortical mastoidectomy, facial recess approach to the cochlea, and placement of the CI receiver/stimulator under skin flap in bone recess. This is followed by preparation of the round window or cochleostomy and appropriate cochlea opening. Subsequent manual insertion of the electrode array is performed into the cochlea by grasping the electrode utilizing one or a combination of instruments or forceps. The surgeon then gently inserts the array by hand under direct microscope visualization for any buckling while avoiding excessive forces per universal insertion principles and specific CI manufacturer guidelines.[17–20] Following CI electrode array insertion, a small fascia graft or muscle plug is placed to seal the cochlea opening to secure the array and the excess electrode lead is additionally secured in the mastoid cavity.[20] The CI ground is then placed in soft tissues at the zygomatic root.

Using the iotaSOFT™ insertion system to assist with electrode array insertion, the surgeon will perform the above described standard surgical approach but will have more speed control of the electrode array insertion and stable trajectory as well as improved consistency of insertion. Should the surgeon need to quickly revert to alternative standard manual insertion techniques at any point during a CI procedure which utilizes the iotaSOFT™ insertion system, this can be accomplished immediately without the need to modify the surgical approach or perform additional surgical steps aside from uncoupling of the iotaSOFT drive head from the CI lead in seconds.

Surgical insertion timing using the iotaSOFT™ insertion system will be evaluated via operative microscope video record analysis. Time stamp mark will start when the electrode begins insertion through appropriate cochlea opening (e.g. through round window or cochleostomy) and end when surgeon determines insertion is complete without further advancement as reviewed on operative microscope recording. The end time will be defined by when the electrode has been inserted fully or the surgeon stops electrode advancement. Should the insertion end due to unanticipated anatomical reasons or significant resistance in insertion, proper adverse event documentation will be completed.

8.2.4 Post-Insertion Electrode Position X-ray Assessment

As per standard of care, following CI electrode array insertion, an intraoperative or post-operative “cochlea view” x-ray via c-arm will be performed to determine radiographically the insertion position of the electrode array and presence of tip-fold.

8.2.3 Post-Activation Impedance and Neural Telemetry

Per current standard of care, post-activation impedance and neural telemetry measurements will be collected at the initial in-clinic activation of the CI (approximately 2 weeks to 1 month following surgery), and at 1-month, 3-months, and 6 months post-activation using the standard non-invasive measurement techniques per CI manufacturer guidelines. Measurement values will be reported via case report form.

8.2.6 Safety Assessments

8.2.6.1 Adverse Events will be reported and documented throughout the duration of the study. All reported events will be recorded on case report forms and determinations will be made as to the whether the events are Adverse Events, Serious Adverse Events, Unanticipated Adverse Device Effects, and/or related to the investigational device or the procedure.

9. STUDY DESIGN

The study is a prospective, single arm, open-label study. Baseline medical data questionnaire will be collected for each subject prior to CI surgery. This will aid in determining adverse events as a result of the study. Aside from the insertion timing, data for evaluation of device safety will be collected after the device has been placed.

9.1 Number of Sites and Subjects

Up to 30 subjects will be enrolled at up to 3 investigational sites. Each site will have adequate facilities for all medical procedures, and sites selected will represent private and larger medical center practice settings. All sites will be required to receive Institutional Review Board (IRB) approval prior to study initiation. Should clearance of the marketing application be received during the study, the Sponsor will determine whether to continue enrolling new subjects. Subjects already enrolled in the study who have not been implanted will be allowed to continue in the study.

9.2 Cochlear Implant Electrodes

Only FDA approved cochlear implant electrode arrays and those validated for compatible use by the iotaSOFT manufacturer will be used for this study, specifically those without a sheath or stylet required for use including MedEl Flex, Cochlear 622/624, and AB Slim J electrode arrays.

9.3 Subject Selection and Withdrawal

Subjects will be screened to verify that they meet all inclusion and exclusion criteria prior to being enrolled in the study. Informed consent will be obtained from every subject as described in Section 13.2 before they are considered enrolled in the study.

9.4 Inclusion criteria

1) Candidate for cochlear implantation according to FDA indications for only the following

electrode arrays**: MedEl Flex, Cochlear 622/624, AB Slim J**

2) Age 18 years or older at the time of enrolment
3) Willingness to participate in and to comply with all requirements of the protocol
4) Fluent speaker of American English due to language used in consent document.

9.5 Exclusion criteria

The Subject must not have known or active medical issues that would preclude having a CI device, including:

1) Prior cochlear implantation in the ear to be implanted
2) Ossification or any other cochlear anomaly that might prevent complete insertion of the electrode array
3) Craniofacial abnormality or Abnormal cochlear/nerve anatomy on pre-operative CT or MRI imaging (excluding a mild Mondini malformation or Large Vestibular Aqueduct Syndrome)
4) Deafness due to lesions of the acoustic nerve or central auditory pathway
5) Diagnosis of auditory neuropathy
6) Active middle-ear infection
7) Additional handicaps that would prevent participation in evaluations
8) Unrealistic expectations on the part of the subject, regarding the possible benefits, risks and limitations that are inherent to the procedure and investigational device
9) Must not fit the definition of a vulnerable subject, as per FDA regulations 21 CFR Parts 50 and 56 [21,22]

10 DETAILED STUDY PROCEDURES

10.1 Candidacy and Enrolment

Once a subject has been determined a candidate for cochlear implantation according to FDA indications the patient will be invited to participate in this study. This will take place at the CI evaluation or the preoperative visit. The subject will be given the Informed Consent and given ample time to review and ask questions (see 13.2 for more information on the consent process). The subject will be given the medical health history questionnaire (FRM00001). Study enrolment will be accounted for on Attachment 6.

10.2 Surgical Preparation

Preparation for surgery will occur as per standard clinical procedures. Surgeons will be trained on iotaSOFT system use and operation with training certification by iotaSOFT manufacturer personnel prior to use, including at least a 1-hour period between training and use of the device. Training will be documented on Attachment 7. Operating room setup and procedure preparation will be followed according to the iotaSOFT™ insertion system instructions for use to ensure the sterile field is not compromised and system is operational (Attachment 8). The operative microscope will be capable of video recording collection. If bilateral cochlear implant

procedure, the first iotaSOFT drive unit will be discarded and new, sterile unit will be used for the contralateral electrode array insertion.

10.3 Surgeon Device Training

Surgeons will be trained on iotaSOFT system use and operation with training certification by iotaSOFT manufacturer personnel prior to use, including at least a 1-hour period between training and use of the device. Training will be documented on Attachment 7.

10.4 Device Surgical Use

CI surgery will be conducted as per each surgeon's standard clinical practice and surgical approach including cortical mastoidectomy and facial recess approach to the cochlea for cochlear implantation. The surgeon then secures the stage base to the skull at superior edge of mastoidectomy with two pre-loaded self-drilling cortical bone screws and supplied sterile screwdriver. The drive unit is placed into the stage base and the adjustable drive head is coupled to a compatible CI silicon lead by clasping clip action onto the CI excess silicone lead away from the electrode array. With manual surgeon manipulation, the drive unit head is positioned outside the facial recess and aligned to the surgeon-desired electrode array insertion trajectory. Before insertion begins, the surgeon selects the desired speed from 0.1mm/sec to 1.0mm/sec in 0.1mm/sec intervals using footpedal controller. With direct access and microscopic view of the surgical site, the surgeon advances or retracts the electrode array via footpedal while guiding the electrode array into the cochlea with standard manual CI instrumentation as necessary. Upon the completion of electrode array insertion and securing the array at the cochlea, the surgeon unclips the drive head and unit from the excess silicone lead then removes the device and screws from the patient for disposal. Per current standard of care, cochlea view X-rays will be performed, and the surgical site is then closed. For detailed device description and professional instructions for use see Attachment 1 & 8.

10.5 Subject Withdrawal or Early Termination

Subjects can choose to withdraw from the study at any time, for any reason, specified or unspecified, and without prejudice. Subjects will be withdrawn from the study for any of the following reasons: termination of study, request by the subject, development of an exclusion criterion prior to CI surgery (i.e., change in ability to meet protocol requirements).

10.6 Medications

No special medications are required for this study. Subjects will follow all standard clinical preparatory surgical procedures given to them by their doctor.

10.7 Protocol Deviations

A protocol deviation refers to a study-related activity that is not in compliance with the investigational protocol. Deviations that are required to protect the life or well-being of a subject do not require prior approval from the Sponsor and should be implemented immediately. The IRB and Sponsor must be notified within 5 (five) days of such an event.

If parts of the study are omitted or completed incorrectly, the event is to be noted on the Protocol Deviation Log provided to the Investigator in the study Regulatory Binder. Depending on the type or severity of the deviation the Investigator may be required to notify the IRB and/or Sponsor if the deviation impacts safety or performance of the subject or data integrity.

10.8 Device Replacements

There is the possibility of device failures (e.g. the iotaSOFT drive unit does not move the electrode as intended, etc), in that case, the surgeon may troubleshoot per instructions for use (Attachment 8), ask for replacement sterile iotaSOFT drive unit, or abandon the study and revert to the standard manual insertion techniques to complete the CI insertion procedure. Such events should be documented.

10.9 Data Identification

Designated study personnel at each site will assign each subject a unique Subject ID identifier. Each case report form will contain this identifier only. Other than the consent form, the names of the subjects will not be documented on any study forms. All consent forms and study-related forms will be archived in a secured area with limited access during the study and upon its completion.

10.10 Accountability Procedures for the Investigational Product

Device accountability will be controlled by documenting (Attachment 9) the dispensing and return of unused devices by designated study personnel.

10.11 Maintenance of Study Randomization Codes

The study will have no treatment randomization. All enrolled subjects will be implanted using the investigational device.

10.12 Identification of Source Data

All study data collected will be source data recorded directly on the CRFs or in the Electronic Database.

11. ADVERSE EVENTS

11.1 Definitions

An Adverse Event (AE) is any untoward medical occurrence in a study subject. This may include illness, sign(s), symptom(s), or clinically significant laboratory test abnormality that has appeared or worsened during the course of the study, regardless of causal relationship to the study device(s) under study.

A Serious Adverse Event (SAE) is any untoward medical occurrence that: results in death, is life-threatening (defined as an event in which the participant or patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe), requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or is an important medical event (defined as a medical event(s) that may not be immediately life-threatening or result in death or hospitalization but, based upon appropriate medical and scientific judgment, may jeopardize the patient/participant or may require intervention (e.g., medical, surgical) to prevent one of the other serious outcomes listed in the definition above. Note: Planned hospitalization for a pre-existing condition without subsequent serious deterioration in health is not considered a serious adverse event.

An Adverse Device Effect (ADE) is any untoward or unintended response to a medical device.

(This includes any event resulting from insufficiencies or inadequacies in the instructions for use or the procedures related to the device.) This includes any AE that is determined to be definitely or probably a result of device use.

An Anticipated Adverse Device Effect (AADE) is an adverse device-related event that has been identified as to the nature, severity or incidence in the protocol.

An Unanticipated Adverse Device Effect (UADE) is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

11.2 Assessment and Recording of Adverse Events

AEs may be either spontaneously reported or elicited during questioning and examination of a participant or discovered during review of the clinical data. All AEs must be reported to the Sponsor by recording them on the Adverse Event form.

The Investigator will decide whether the particular problem is investigational device-related or not and record his/her decision on the AE form. The relationship to the study product or procedure will be determined by the Investigator, as being: a) definitely related, b) probably related, c) possibly related, d) unlikely related or e) not related.

If an event is deemed serious, such events will be reported to the Sponsor via the completion of the Serious Adverse Event CRF.

11.3 Procedures for Reporting Adverse Events

Adverse events classified as "serious" or “unanticipated” (SAEs or UADEs) will be reported promptly to the IRB and study Sponsor to comply with regulatory requirements. All serious AEs, whether related or unrelated to the device, as well as all UADEs, will be immediately reported (but in no event later than 2 working days after the Investigator first learns of the event) to the Sponsor by telephone or confirmed facsimile or email transmission.

The Sponsor will immediately conduct an evaluation of any unanticipated adverse device effect. If the Sponsor determines that an unanticipated adverse device effect presents an unreasonable risk to subjects, the Sponsor will terminate all investigations or parts of investigations presenting that risk as soon as possible. Termination will occur not later than 5 working days after the sponsor makes this determination and not later than 15 working days after the sponsor first receives notice of the effect.

As required, the Sponsor will summarize all reported AEs that are serious, unexpected, and certainly, probably, possibly, or of undetermined relationship to the device. This information will be provided to the FDA (by the sponsor) and to the IRB by the Investigator or designee, as appropriate.

12. QUALITY CONTROL AND QUALITY ASSURANCE

Accurate, consistent, and reliable data will be ensured through the use of standard practices and procedures. All of the Data Management, query resolution, Monitoring, etc. will be

managed by iotaMotion, Inc. These are described in the following sections.

12.1 Direct Access to Source Data/Documentation

The investigators and accompanying institutions will agree in writing to allow study-related monitoring and audits by the Study Sponsor, or designee, and regulatory authorities. The IRB and FDA will have the authority for regulatory review and inspection(s) by being allowed direct access to the source data and related documentation.

12.2 Data Collection, Monitoring, and Transfer

The investigators and study personnel will perform data collection. The Sponsor will perform all monitoring and data transfer tasks. A Monitor designated by the Sponsor will be responsible for monitoring the clinical study in accordance with current federal and relevant foreign regulations. Monitoring dates will be documented on Attachment 10. A monitoring plan for the study will be developed by the Sponsor.

12.3 Data Management

The study Monitor will review all consent forms, CRFs, Electronic database entries, and related reports including adverse event reports consistent with the monitoring plan. These will form the basis for all data analysis related to this study. All data will be scanned or keyed into a computer system or electronic database for direct access and for subsequent reports. A clinical review will be performed by the Sponsor to identify those minor issues that otherwise remain unresolved.

13. ETHICS

13.1 Compliance Statement

The study will be conducted in accordance with the approved study protocol and applicable regulatory requirements as described in the United States Code of Federal Regulation (CFR) 21 Parts 50, 54, 56, and 812.[21–23] As required by 21 CFR Part 50 and Part 56 and the Declaration of Helsinki, the study protocol, amendments, and Informed Consent form will be reviewed and approved by each study center's IRB or an appropriate independent IRB prior to study initiation at that site.

13.2 Subject Information and Consent

The written Informed Consent forms will meet requirements for subject information, as outlined in FDA regulations (21 CFR Part 50),[21] and the Declaration of Helsinki. Informed consent will be obtained from every subject in a manner compliant with 21 CFR Part 50 before any testing is done. The information will be presented verbally as well as in a written document. The Informed Consent form will be signed by each subject. A copy of the signed consent form will be given to each subject.

13.3 Compensation, Insurance and Indemnity

Financing and insurance will be addressed in separate agreements with the investigator(s)/institution(s). The subject will not be compensated for participating in the study as detailed in the Informed Consent. In case of injury related to this research, the subject will be appropriately treated by the study doctors without cost to the subject. If the subject seeks alternative medical treatment, that treatment will be billed to the subject's health insurance and

will not be paid by iotaMotion, Inc. The company will not pay for lost wages or other financial compensation for injury.

14. STUDY REPORT AND PUBLICATION PLAN

iotaMotion, Inc. will own the data generated from this prospective study and the study devices. The Principal Investigator will be responsible for publishing or presenting any findings in accordance with the Investigator Agreement. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law.

15. ATTACHMENTS

15.1 Attachment 1 – Detailed Device Description

15.2 Attachment 2 – 720-036-0031 – Bench Performance Testing Report

15.3 Attachment 3 – 722-036-0021 – Benchtop Comparative Analysis Report

15.4 Attachment 4 – 722-036-0020 – Cadaveric Comparative Analysis Report

15.5 Attachment 5 – 712-036-0010 – Usability Validation Report

15.6 Attachment 6 – Study participant log

15.7 Attachment 7– Investigator training log

15.8 Attachment 8 – Professional instructions for use

15.9 Attachment 9 – Device accountability log

15.9 Attachment 10– Study monitoring plan

15.10 FRM00001– Medical History form

15.11 FRM00002 – Surgical Questionnaire

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20. MedEl Mi1250 Synchrony 2 Surgical Guide.
21. 21 CFR Part 50: Protection of Human Subjects.
22. 21 CFR Part 56: Institutional Review Boards.
23. 21 CFR Part 812: Investigational Device Exemptions.