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D1.3– DATA MANAGEMENT PLAN

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D1.3 DATA MANAGEMENT PLAN

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VERSION	CREATED/MODIFIER	COMMENTS
0.0	Emilie BLOTIERE (INRIA)	First draft
	Christine AZEVEDO COSTE (INRIA), David GUIRAUD (NEURINNOV), Camille MARQUEZ (NEURINNOV), Thomas GUIHO (INRIA), François BAILLY (INRIA), Thomas STIEGLITZ (UFR/IMTEK), Danesh ASHOURI (UFR/IMTEK), Charles FATTAL (UFR/IMTEK), Frédéric DIERICK (Rehazenter), Vera OPPELT (CorTec GmbH), MARTIN SCHUETTLER (CorTec GmbH), ARTHUR UNTCH (CorTec)	Contributors
0.1	Christine AZEVEDO COSTE (INRIA), Camille MARQUEZ (NEURINNOV), Emilie BLOTIERE (INRIA)	Review
1	Emilie BLOTIERE (INRIA)	Final version

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TABLE OF ACRONYMS

AIMD	Active Implanted Medical Device
BIL	Base Information Logiciel (Software Information Base)
CA	Consortium Agreement
CAMIN Team	Artificial Motion Control and Intuitive Neuroprostheses
CT	Clinical Trial
ES	Electrical Stimulation
FIM	First-in Man trial
GA	Grant Agreement
GDPR	General Data Protection Regulation
INRIA	Institut National de Recherche en sciences et technologies du numérique
IP	Intellectual Property
HMI	Human Machine Interface
MIR	Medical Imaging Resonance
NCA	National Competent Authority
NFDI	National Research Data Infrastructure
PNS	Peripheral Nervous System
WP	Work Package

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ABSTRACT

The AI-Hand Data Management Plan (DMP) provides information regarding the collection, management, and processing of research data collected and/or produced during the project, and outlines measures to make this data FAIR (findable, accessible, interoperable, reusable). This document constitutes the initial version and has been elaborated as a deliverable (D1.3). This report covers data management procedures applicable to all consortium members. This initial version will be updated twice during the periodic reports in M30 and in M42 in an iterative process. It is led by the coordinator and completed by each partner to describe the data treatment in each WP.

Whenever necessary or required, the content will be adjusted or supplanted by the consortium to suit the technical and administrative purposes of the AI-Hand project as it evolves over its lifetime.

The AI-HAND project proposes radically new paradigms of electrical stimulation (ES) of the peripheral nervous system (PNS) requiring disruptive methods and technologies that will open breakthrough therapeutic perspectives. To date, patients with a complete quadriplegia has no solution to restore hand movements; they will be the first to benefit from AI-HAND new approach. Indeed, multiphasic stimulus waveforms, multiple synchronized currents sources for 3D current shaping over a multi contact neural cuff electrode and complex interleaved stimulation instead of standard rectangular single-source sequenced stimulation, are the strong breakthrough innovations proposed that allow to answer unmet needs in a wide range of medical applications.

Besides, the Active Implanted Medical Device (AIMD) research and industry are highly conservative as both innovation and regulation demand a strong effort and a long-term vision to go a step further. AI-HAND thus proposes to implement the cutting-edge findings in electrophysiology through radically innovative, fully safe and software-free implant technologies that would lead to a generic powerful new generation of AIMD.

The project is funded under the Horizon Europe Framework Programme (Horizon Europe) and started 1st August 2023 for 42 months It gathers six European partners:

- INRIA, the coordinator, the French national institute in computer science and new digital technologies
- Neurinnov, a French private developer of advanced neurostimulation solutions
- Rehazenter, the National Center for Functional Re-education and Rehabilitation in Luxembourg
- USSAP, the health and social union for support and prevention in France
- UFR, Albert-Ludwig University in Freiburg in Germany,
- CorTec GmbH as an affiliated entity, a private company, provide components, interfaces and active systems to enable the communication with the brain or other parts of the nervous system

The project implies ethical dimensions as the final objective is to implant an AIMD in four persons with complete tetraplegia (WP7). A clinical trial that involved the not only ethics committee approval but also National Competent Authority approval (NCA) is envisioned for this First in Man trial (FIM). Two preliminary clinical trials will also be performed to validate some of the proposed approaches with non-

implanted technology (WP6). The consortium follows the European legislation the MDR 2017 / 745[1] and ISO 14155-2020[2]. The consortium is aware of all the procedures and has a long experience in carrying trials with humans including invasive ones. The consortium already succeeded in similar protocols to obtain clearance of both instances recently. The application is prepared already in order to answer timely to the questions issued by these committees. Preclinical studies in pigs are planned in WP5.

[1] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32017R0745

[2]https://ceiso.fr/wp-content/uploads/2023/03/CL06_Programme_Investigations-cliniques-et-Bonnes-Pratiques-Cliniques-selon-la-norme-ISO-14155.pdf

INTRODUCTION

The AI-Hand Data Management Plan[3] (DMP) includes information on:

- the handling of scientific data during and after the end of the project
- what data will be collected, processed, and/or generated
- which methodology and standards will be applied
- whether data will be shared/made open access
- how data will be curated and preserved (including after the end of the project).

The Ai-Hand DMP is based on the Horizon Europe Data Management Plan Template (version 1.0, 05 May 2021). The DMP is envisioned to be a living document and, over the course of the project, the DMP will be updated if significant changes arise. All changes to the DMP will be noted in a "History of Changes" table to be included in the annex of all updated versions. The Ai-Hand DMP follows the definition of research data and research data management as outlined in the "Practical Guide to the International Alignment of Research Data Management - Extended Edition"[4] of 2021 by Science Europe.

The DMP takes GDPR (General Data Protection Regulation) compliance and the minimum FAIR[5] requirements into account.

[3] In compliance with the Horizon Europe Data Management Plan Template (version 1.0 5 May 2021)

[4] Science Europe. "Practical Guide to the International Alignment of Research Data Management - Extended Edition". 2021. https://doi.org/10.5281/zenodo.4915861.

[5] See more on the FAIR principles: https://www.go-fair.org/fair-principles

I. DATA SUMMARY

AI-Hand collects and generates different types of data including sensitive ones which require a specific treatment before and after the collection. In the current DMP, Data is understood as any scientific or technical data, including the Personal Data and clinical Data, that is owned or stored by a partner prior to the project start or that is generated under the project.

So far four main categories were identified:

● Research or scientific data related to the four protocols that are planned during the project and more precisely, the non-invasive trials on human beings (CT1 and CT2), the invasive experimentations on animals and finally the First In Man trial planned M18 with tetraplegic participants (FIM).

● Technical data related to the technological developments and performances

● Clinical data related to information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Clinical data is contained in source documents corresponding to original documents, data, and records (e.g.: hospital records, clinical and office charts, laboratory notes, memoranda, subjects' diaries or evaluation checklist, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial). Clinical data to which another partner may have access is pseudonymized data. The Clinical data generated during the clinical trials remains under the sole direction, custody and responsibility of the sponsor (e.g., the data owner).

● Health data is broader than diagnostic elements or symptoms. Health data includes all data from which it is possible to deduce information about a person's state of health as for instance: the name of a patient with appointments, an address in a specialised accommodation and a hospital admission number.

● Personal data related to an identified or identifiable living individual. Different pieces of information, which collected together can lead to the identification of a particular person, also constitute personal data. Personal data that has been de-identified, encrypted or pseudonymised but can be used to re-identify a person remains personal data and falls within the scope of the GDPR.

The project collects and generates meaningful data including ones falling into specific categories of personal data as described within the General Data Protection Regulation (GDPR)[6]. Data may be quantitative or qualitative and are analysed from a range of methodological perspectives with a view to producing insights that feed the project activities, enabling the consortium in delivering relevant input.

The detailed protocols are currently being drafted; the document will be updated once the exact content is decided.

[6] https://gdpr-info.eu/

A. Animal experiment protocol

Data category	Anatomo-physiological data from pigs
Data type	All Data that will be generated during the project including: Stimulation logs Electrophysiological measurements: - Biological signals: Evoked-muscular activity (Electromyography – EMG) & Evoked-neural activity (Electroneurography – ENG) - Videos and pictures of the experimentations - Tissue samples - Histology of nervous tissue
Data formats	Stimulation logs (.txt); Biological signals (.txt, .dat ou .hdf5); Videos (.avi or .mp4) ; Histological images (.jpeg ou .png).
Size	Logs: 500 Mo; Biological Signals: 500 Go; Videos: 50 Go; Histology: 1 Go
GDPR issues	No except the personal data of the surgical team (Name, contact, CV) Experiments will be performed with the approval of Animal Welfare and Ethical Review Boards
Data collection purpose	1) Optimization of peripheral nerve stimulation for scientific publications purposes (INRIA) 2) Validation of the performance of the implant & Long-term biocompatibility of the implant (NEURINNOV)
Accessibility level	1) To be decided later 2) No accessibility: trade secret

B. Human clinical trials protocol CT1

Data category	Motion Data
Data type	Kinematics, Electromyography (EMG) & Force; Video/Pictures
Data formats	txt; avi; mp3
Size	1Go; 10Go; 5 Go
GDPR issues	Yes – Personal data + Videos&Pictures
Data collection purpose	Assessing performances in using new sensors to control target on the screen
Accessibility level	Anonymised motion data (kinematics, forces) may be shared with scientific community

Data category	NEURINNOV Sensor trial data on human
Data type	Data generated during the project: Clinical: - Auto evaluation from patients - Personal data from medical staff (Name, contact, CV, voice, image)

	- Personal data from patients (Age, medical situation, life habits, voice, image, spinal cord lesion characteristics) - Personal data from helpers (Age, life habits, voice, image) **Technical:** - Raw data from EMG, IMU, voice - Technical logs - Technical data for machine learning - Videos and pictures of the experimentations
Data formats	Log and reports: .txt and .pdf; video: .mp4 or .avi; picture: .png; raw data audio: .wav (voice); Data for machine learning: .dat
Size	Log and reports: 500 Mo; video: 10 Go; picture: 1 Go; raw data audio: 100 Go; Data for machine learning: 100 Go.
GDPR issues	Yes – Videos of patients and voice. Personal data from patients, helper and medical staff.
Data collection purpose	Evaluate what sensor is the best for the patient. Evaluate the clinical performance of the sensor. Evaluate if the patient can put himself or herself the sensor. Technical performance: success rate Evaluate the patient's satisfaction.
Accessibility level	No accessibility: trade secret Partial protocol on public trial registers

C. First in Man protocol

Data category	Clinical investigation human data
Data type	**Data generated during the project:** **Clinical:** - Auto evaluation from patients - Personal data from medical staff (Name, contact, CV, voice, image) - Personal data from patients (Age, medical situation, life habits, voice, image, spinal cord lesion characteristics) - Personal data from helpers (Age, life habits, voice, image) - Usability reports from the users **Technical** - Raw data from EMG, IMU, voice - Stimulation configuration (linked to patient) - Implantation report (linked to patient) - Videos: Elicited movements; patient training - Technical log - Impedance

	Videos and pictures of the experimentations Data created before the experimentation: - Accompanying documentation - IFU Data from technical file: - Risk management report - Usability report - Conception file
Data formats	Log and reports: .txt and .pdf; video: .mp4 or .avi; picture: .png; raw data audio: .wav (voice); technical data: .dat
Size	Log and reports: 500 Mo; video: 10 Go; picture: 1 Go; raw data audio: 100 Go; technical data: 100 Go.
GDPR issues	Yes – Videos of patients and voice. Personal data from patients, helper and medical staff.
Data collection purpose	Evaluate the safety and the performance of the entire medical device
Accessibility level	No accessibility: trade secret Partial protocol on public trial registers

D. CorTec

Data category	**Electrode Data**
Data type	Impedance Data
Data formats	Log and reports: .txt, .xlsx, .csv
Size	technical data: 100 Go
GDPR issues	No
Data collection purpose	Evaluate performance of electrodes for future improvements
Accessibility level	Anonymised impedance data

E. UFR/IMTEK

Data category	**Characterization of Electrode and Cable stability**
Data type	Readouts from validation steps to assess reliability and stability of cables, connectors and the cuff interface: Impedance, Cyclic Voltammetry, Force, Elongation, SEM images, ToFSIMS, EDX
Data formats	Machine output data: .txt, xlsx, .csv, .jpeg
Size	100 GB
GDPR issues	None
Data collection purpose	Evaluate the safety and the performance of the electrode/cables/ connectors
Accessibility level	Initially no shared data, but available on request by partners in connection with publication output when not in conflict with potential IP protection. This will be assessed on a case-to case basis. In case of patent registration, data will be available to project partners upon request.

F. Rehazenter

Data category	Clinical investigation human data
Data type	**Data generated during the project:** **Clinical:** Auto evaluation from patients Personal data from medical staff (Name, contact, CV, voice, image) Personal data from patients (Age, medical situation, life habits, voice, image, spinal cord lesion characteristics) Personal data from helpers (Age, life habits, voice, image) Usability reports from the users **Technical** - Raw data from EMG, IMU, voice - Stimulation configuration (linked to patient) - Implantation report (linked to patient) - Videos: Elicited movements; patient training - Technical log - Impedance Videos and pictures of the experimentations Data created before the experimentation: - Accompanying documentation - IFU Data from technical file: - Risk management report - Usability report - Conception file
Data formats	Log and reports: .txt and .pdf; video: .mp4 or .avi; picture: .png; raw data audio: .wav (voice); technical data: .dat
Size	Log and reports: 500 Mo; video: 10 Go; picture: 1 Go; raw data audio: 100 Go; technical data: 100 Go.
GDPR issues	Yes – Videos of patients and voice. Personal data from patients, helper and medical staff.
Data collection purpose	Evaluate the safety and the performance of the entire medical device
Accessibility level	No accessibility: trade secret Partial protocol on public trial registers

G. USSAP

Data category	Clinical investigation human data
Data type	Data generated during the project: Personal data from medical staff (name, personal details, CV, voice, image) Clinical: - Personal data from patients (age, clinical characteristics, life habits, voice, image) - Personal data from helpers (age, life habits, voice, image) - Patients self-reported outcomes - Patients' self-perception well-being - Functional assessment - Usability assessment - Reproducibility of controlling electrical stimulation of the hand (IMU, EMG, voice) - Safety data relating to the surgical and experimental procedure Technical: - Raw data from EMG, IMU, voice - Stimulation configuration (linked to patient) - Implantation report (linked to patient) - Videos: Elicited movements; patient training - Technical log - Impedance Videos and pictures of the experimentations Data created before the experimentation: - Accompanying documentation - IFU Data from technical file: - Risk management report - Usability report - Conception file
Data formats	Log and reports: .txt and .pdf; video: .mp4 or .avi; picture: .png; raw data audio: .wav (voice); technical data: .dat
Size	Log and reports: 500 Mo; video: 10 Go; picture: 1 Go; raw data audio: 100 Go; technical data: 100 Go.
GDPR issues	Yes – Videos of patients and voice. Personal data from patients, helpers and medical staff.
Data collection purpose	First in Man clinical trial
Accessibility level	No accessibility: trade secret Partial protocol on public trial registers

II. FAIR DATA

A. Making data findable, including provisions for metadata

As often as possible, AI-Hand consortium gives open access to the data generated or re-used during the course of its activities. Open data produced during the implementation of the project are locatable by means of a standard identification mechanism. The consortium strives to make project data available as open access to the furthest extent possible while accounting for specificities of IP protection and confidentiality requirements of its industry partners. At the same time, non-opened data will be deposited in a searchable resource and well-tailored identification mechanisms will be utilised as well, in the form of standard naming conventions that will safeguard their consistency and make them easily locatable for partners within the frame of the project. For confidential and non-opened data, each beneficiary uses the secured local host of their institutions as described in the table below.

INRIA	Some data from pig experiments (electrophysiology, movement) as well as data from human experiments (anonymized movement kinematics and dynamics data) may be opened (reusable to other researchers). Pig data and non-clinical pseudonymized human data will be saved in a dedicated INRIA encrypted server accessible to specific persons only.
NEURINNOV	For clinical investigations for which Neurinnov is the sponsor, partial protocols will be published on the national registers of protocol submissions. Nonclinical data are stored on the Neurinnov' data storage solution (kDrive – Swiss Datacenter) and clinical data will be store on a future storage solution, HDS certificated. The identification and contractualization with this subcontractor are on progress and will be achieved before the clinical trials.
UFR/IMTEK	Technical data on electrode characterization (electrical, electrochemical, mechanical, chemical composition, imaging) will be acquired via benchtop tests from virgin as well as from explanted electrodes. IMTEK follows the University of Freiburg (UFR) storage rules of data. Data will be stored on a central university server with daily backups according to the procedures defined the laboratory's ISO 13485 quality management handbook. Server accessibility only for project and management personal. UFR is part of the NFDI (Nationale Forschingsdateninfrastruktur; National Research Data Infrastructure) in which a national research infrastructure is set up to allow for sustainable data use. The identification of the data follows the consortium agreement. Data access might be given on request according to publication rules fulfilling all requirements of the consortium agreement.
USSAP	Patient data is sensitive personal health data and is treated as such. This means that none of this data is intended to be open. Clinical data are written down on paper and at the end of the study, the observation files are digitised and stored on the personal

	patient file on USSAP datacentres, in France. This server is HDS certified. Clinical data are identifiable thanks to the patient identifier. Protocols are opened and will be available on Clinicaltrials.gov.[7]
REHAZENTER	Technical data pertaining to technological advancements, including solution design and operational modes, is made accessible for reuse by fellow researchers. Clinical data is securely stored in a restricted-access folder on the Rehazenter server, utilizing robust access controls, and premises are maintained through guarding measures. The server is on-premises, accessible exclusively from the internal network or through WorkSpace ONE. The access to clinical data is restricted to an Active Directory account, and the permissions for directories/files are administered by the Rehazenter through groups in the Active Directory. A correspondence table, accessible solely by one researcher through a password-protected mechanism, facilitates the mapping of unique identifiers to the actual data. Each patient is associated with a unique identifier, ensuring traceability without compromising individual identities. Only pseudonymized data is transmitted during project-related data transfers, ensuring the confidentiality of sensitive information.
CorTec GmbH	(Pre-)Clinical electrode impedance data are stored on the CorTec's data storage solution (server accessibility only for project and management personal). The identification of the data follows the consortium agreement.

Table 1 Making data findable

B. Making data accessible

The AI-Hand consortium collects a variety of data, which have different natures and access privileges. This section defines the different levels of confidentiality that may exist within the project. According to the long-term data utility and potential limitations due to the protection of personal data, different levels of confidentiality are considered within the project consortium:

- Confidential to partner. This option is applied when the case is tied to a data that is collected by a specific partner and that contains personal data that cannot be protected once disclosed.
- Confidential to consortium members. This option is applied or data containing confidential information or those with no wide-scope of use and long-term value.
- Public

The data collected during the progress of the tasks are initially stored locally by the partner who collected them. It is classified as "confidential to partner" and be used for the restricted purpose of this project only. Like all confidential data in AI-Hand, its preservation and maintenance during and after the project will be handled by the data owners. The consortium members will have to select an option among the following:

- Open Access. This is the highly recommended option which provides free access and rights to data. This is mandatory under the Horizon Europe funded programme and described in the EU Grants AGA[8].

[7] https://clinicaltrials.gov/

[8] EU Grants: AGA – Annotated Grant Agreement: V1.0 DRAFT-01.04.2023

- Embargoed Access. This option concerns data underpinning publication. Data will indeed be deposited as soon as possible but open access will be provided only once the data has been published in a scientific paper to preserve the authorship of all authors involved. In such case, information about data will be published and details of when the data will become available will be included in the metadata.
- Restricted Access. This option, although not recommended, will be adopted for those data with an access that should be monitored and approved by the depositor if certain requirements to be defined are met.
- Closed Access. This option concerns private (but not confidential) data.

Although the embargoed or closed access options could be a valid choice, the consortium agrees that the confidential data and datasets to be collected will not be deposited to avoid compromising their protection or commercialisation prospects.

Since data management concerns clinical trials, and a few patients will be included, open access to all data won't be allowed due to potential identification, GDPR and National Data Protection authority (as for instance CNIL[9] for France and CNPD[10] for Luxemburg) are applied, patient's data linked to health state are solely stored by clinics.

Research data are defined as factual records in the form of figures, texts, images and sounds which are used as the main sources for scientific research and which the scientific community generally recognises as being necessary to validate research results. The OECD gives a definition of research data in its 2007 report 'Principles and Guidelines for Access to Research Data from Public Funding'[11]: Research Data Gouv makes final research datasets available. These datasets are in open access or shared on a restricted basis if there are legitimate legal exceptions like professional secrecy, industrial and commercial secrets or in the case of personal data. The data management clusters support research teams throughout the data lifecycle. However, the Research Data Gouv data repository and registry just provides support for the downstream part of the data lifecycle involving the dissemination of final data sets. The first third of this cycle covers the stages of data collection, creation, storage and processing which are all aimed at producing scientifically validated data. These stages are worked on in laboratories using storage and calculation services. The Recherche Data Gouv data repository does not represent a storage solution for data that are still being processed. Recherche Data Gouv's involvement begins with the second third of the data lifecycle. This involves the curation, deposit and publication of approved final scientific data and the curation of datasets through checking the metadata and data files deposited in the repository. Recherche Data Gouv also works on the final third of the data lifecycle. This consists of disseminating citable data by opening, sharing (restricted access) and making data available for reuse. The Recherche Data Gouv data repository offers a sovereign multi-disciplinary repository for publishing data sets. The

[9] https://www.cnil.fr/en/official-texts
[10] https://cnpd.public.lu/fr.html
[11] https://www.oecd.org/sti/inno/38500813.pdf

platform is designed to meet the needs of communities not yet equipped with a recognized thematic repository. Data that have already been shared or made available through an established thematic repository, either in France or abroad, can also be reported in the Recherche Data Gouv registry.

INRIA	Data produced and deemed open for sharing and re-use are deposited to and securely stored on secured INRIA software. Open datasets are deposited on French "Research Data Gouv" platform[12] , a national and secured Open Science repository. The Research Data Gouv multidisciplinary repository is a sovereign solution for sharing and opening up data produced by communities that do not have a recognized disciplinary repository. It is based on the Dataverse software.
NEURINNOV	Neurinnov is a company and designs and develops a medical device and its accessories for marketing under Regulation (EU) 2017/745. The data generated by the AI-HAND project are used in the technical documentation for CE marking. Under these conditions, the data is not intended to be accessible by research teams. For clinical investigations for which Neurinnov is the sponsor, partial protocols will be published on the national registers of protocol submissions.
UFR/IMTEK	As a University Institute, IMTEK is part of the NFDI (national research data infrastructure) that is currently under establishment. Goal of the NFDI is sustainable storage and sharing of data. Until this structure is running, general scientific data is stored on servers of the university with access of the laboratory members involved in AI-Hand at IMTEK. Access is controlled by university rules and measures based on the specific personal access rights and ends after contract termination with the university. Data will be stored at least until 2032 on the university servers. Acquired impedance data can be accessible without allocation of patient related data. Data access is only available through management permission. Initially no shared data, but available on request by partners in connection with publication output when not in conflict with potential IP protection of. This will be assessed on a case-to-case basis where data are available to project partners upon request. Access is managed by Thomas Stieglitz (thomas.stieglitz@imtek.uni-freiburg.de). IMTEK will envision open access publications and will make data available within publications in accordance with terms and conditions of the Consortium Agreement.
USSAP	Clinical data are protected by medical secret. Therefore, they are not opened. The clinical data are stored on secured repository certified HDS. The HDS certification is available on demand.
REHAZENTER	Data generated by the project serves the assessment of the safety and overall performance of the entire medical device. The processed data encompasses auto-evaluations from patients, personal data from medical staff (including name, contact, CV, voice, and image), personal data from patients (covering age, medical situation, life habits, voice, image, and spinal cord lesion characteristics), and personal data from helpers (including age, life habits, voice, and image). This comprehensive dataset serves as a primary source for scientific research and is widely recognized by the scientific community as essential for validating research results.

[12] https://recherche.data.gouv.fr/en/page/which-research-data

	The data produced by Rehazenter will be stored on the secured Rehazenter information system. This rigorous approach ensures full compliance with privacy regulations while making a substantial contribution to scientific advancements.
CorTec GmbH	Patient related data will not be raised. Acquired impedance data can be accessible without allocation of patient related data. Impedance data underlies CorTec's interest and is therefore not opened but stored in CorTec's data management system. Data access is only available through management permission.

Table 2 Making data accessible

C. Making data interoperable

AI-Hand project aims to collect and document the data in a standardised way to ensure that the data and datasets can be understood, interpreted, reused, and shared in isolation alongside the accompanying metadata and documentation. Standard vocabulary will be used for all data types present in the dataset to allow interdisciplinary interoperability. In addition, whenever required, the documentation will include a general glossary used to share information about the vocabulary and general methodologies employed for the generation of the data.

INRIA	uses standardised formats e.g. .txt, .xlsx, .csv, .jpeg
NEURINNOV	uses standardised formats e.g. .txt, .xlsx, .csv, .jpeg.
UFR/IMTEK	uses standardised formats e.g. .txt, .xlsx, .csv, .jpeg.
USSAP	uses standardised formats e.g. .txt, .xlsx, .csv, .jpeg
REHAZENTER	In Rehazenter, data interoperability is ensured by adhering to widely accepted formats and standards. Non-opened data is stored in secured and standardized databases, ensuring seamless integration and compatibility with various analytical tools and platforms.
CorTec GmbH	uses standardised format e.g. .txt, .xlsx, .csv

Table 3 Making data interoperable

D. Increase data re-use

The collected public data are openly available, once ready for dissemination. To allow the widest possible reuse, the consortium will attach a specific license to every deposited data or dataset. This will allow indeed the definition of all the work conditions as being under an open or a restricted access. INRIA follows five different licensing options among Creative Commons (CC) Licenses, all foreseeing the attribution requirement to appropriately credit the authors for the original creation. Whenever possible, the Creative Commons Attribution 4.0 International (CC BY 4.0) license will be used, in order to allow third parties to share and adapt data with no restrictions if attribution is provided. In case the partner

would like to further limit access to the uploaded data, an alternative license will be selected among the following options:

- Creative Commons Attribution Share-Alike 4.0 International (CC BY-SA 4.0). Allows modification of the data for any purpose as long as it is distributed under the same original license (or a license listed as compatible).
- Creative Commons Attribution-NoDerivatives 4.0 International (CC BY-ND 4.0). Allows distribution of the data for any purpose, but forbidding the distribution of derivative work.
- Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0). Allows sharing and modification, but limiting use to non-commercial purposes.
- Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NCND 4.0). Allows sharing but restricting both derivative work and commercial use of data.
- Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International (CC BY-NC-SA 4.0). Allows modification as long as it is distributed for non-commercial purposes and under the same original license (or a license listed as compatible).

A Readme file accompanies open data and is accessible on Research Data Gouv for facilitating the data reuse. UFR/IMTEK promotes the idea of open science and open data but does not yet have a general guidance on open access licenses. Therefore, open access will be granted when structures have been harmonized on the university level.

III. OTHER RESEARCH OUTPUTS

Software description	Generated or re-used?	Why is this code generated?	Is the code source open or close	Location of the code source	What institution harvests the code source?
IMUSEF: software interface for the control of external FES devices BIL repository : https://bil.inria.fr/fr/software/view/3520/tab	Reused	WP5	No access is given to Source code.	Gitlab	INRIA
I-GRIP: software for computer-vision based automatic grasp selection BIL repository : https://bil.inria.fr/fr/software/view/4891/tab	Reused	WP6	No access is given to Source code.	Gitlab	INRIA
MOS2SENS: Model Optimization and simulation to Selective Electrical Neural Stimulation Bil repository : https://bil.inria.fr/fr/software/view/1681/tab#	Reused	WP5	No access is given to Source code.	Gitlab	INRIA
Hand simulator	Generated	WP6	No access is given to Source code.	Gitlab	INRIA
Clinical interface for online assessment of hand gestures	Generated	WP6	No access is given to Source code.	Gitlab	INRIA NEURINNOV
Neurisoft: Medical device software for the implant configuration during the implantation	Generated	See description	No access is given to Source code	Neurinnov closed GitHub	NEURINNOV
Neurisence: Medical device software for patient training after the implantation	Generated	See description	No access is given to Source code	Neurinnov closed GitHub	NEURINNOV
Script Neurinnov: gestion and transformation of raw data	Generated	See description	No access is given to Source code	Neurinnov closed GitHub	NEURINNOV
CorTec	n/a	n/a	n/a	n/a	n/a
Rehazenter	n/a	n/a	n/a	n/a	n/a
USSAP	n/a	n/a	n/a	n/a	n/a
UFR	n/a	n/a	n/a	n/a	n/a

Table 4 Software description

Other expected outputs

Nature of the output	Description	Describe the process of information	Describe the output data	Is the data openly circulated ?
Workflow	In vivo validation of stimulation tools developed by Neurinnov (WP5)			
Workflow	Improved paradigms for selective peripheral nerve stimulation			
Workflow	Development and improvement of electrophysiological signal processing algorithms (in collaboration with Neurinnov)			
Workflow	Force feedback for versatile grasp (WP6)	Grasp force is estimated and displayed on a screen. User controls the force by increasing or decreasing the stimulation intensity using available sensors.	Assessment of the difference between targeted force and real force.	Data available to partners on demand.

Table 5 Other expected outputs

IV. ALLOCATION OF RESOURCES

Responsible for the data management is Christine Azevedo Coste (christine.azevedo-coste@inria.fr).

As for the collected data tied to the confidential datasets, each partner is responsible for its collection. Therefore, its maintenance, backup and versioning and long-term preservation and archival is guaranteed by the partners' own resources and at their own expense.

The additional costs foreseen for data management are indeed related to:

- The working time to set up and perform data collection and analysis activities
- The working time to set up and maintain local and shared data collection devices/servers.
- The working time needed to write documentation, metadata etc.

The project coordinator is in charge of the DMP from both the scientific and technical perspective. The registration of datasets and metadata, as well as backing up data for sharing through open access repositories, is the responsibility of the partner that gathers the data in its related work package. Quality control of these data is the responsibility of the relevant work package leader, supported by the Project Coordinator.

Each partner should respect the policies set out in this DMP.
Publications featuring the data will be produced in the project and will be made available in open access on Research Data Gouv, and Alfresco SHARE, by selecting journals or conferences allowing immediate public access on institutional repositories, open access journals, or journals or conferences featuring a short embargo period. Possible costs related to open access will be claimed as part of the Horizon Europe grant.
Finally, in line with the Consortium Agreement, each partner should give at least 30 days prior notice to the other partners before disseminating/publishing data.

V. DATA SECURITY

Institution	Non opened data storage
INRIA	Pig data and non-clinical pseudonymized human data will be saved in dedicated INRIA encrypted server accessible to specific persons only
Neurinnov	Non clinical data are stored on the Neurinnov' data storage solution (kDrive – Swiss Datacenter) and clinical data will be stored on a future storage solution, HDS certificated. The identification and contractualization with this subcontractor are on progress and will be achieved before the clinical trials.
Rehazenter	Personal data will be saved in Rehazenter on-premises secured server accessible to specific persons only. The server is accessible exclusively from the internal network or through WorkSpace ONE. The access to clinical data is restricted to an Active Directory account, and the permissions for directories/files are administered by the Rehazenter through groups in the Active Directory.
UFR/IMTEK	Electrode data will be stored on university servers with access for laboratory members (project and management personal).
USSAP	In USSAP local secured servers
CorTec GmbH	(Pre-)Clinical electrode impedance data are stored on the CorTec's data storage solution (server accessibility only for project and management personal).

Table 6 Non-opened data storage

Accessibility of non-opened data	
INRIA	A list of engineers and researchers is specified to request access
NEURINNOV	Nonclinical data are accessible to Neurinnov' employees. Clinical data are restricted to a limited number of Neurinnov' employees according to their missions. This list has to be defined.
UFR/IMTEK	Non clinical data is accessible to IMTEK employees. Non open data is restricted to project and management personal.
USSAP	A restricted list of identified people has access, internal to USSAP
REHAZENTER	Yes, a specific list includes one physician and two researchers
CorTec GmbH	Non clinical data is accessible to CorTec's employees. Non open data is restricted to project and management personal. Traceability of access guaranteed by access permission through management.

Table 7 Non-opened data accessibility

Process to protect and pseudonymize data	
INRIA	An identification code of the participant is delivered by the promotor of the study. No corresponding table is stored.
NEURINNOV	The pseudonymization process is planned to be used, but the design of the process itself is still ongoing, and depends on the solution of HDS datacenter chosen. The process will be described in a future version of the DMP.
UFR/IMTEK	No access to patient data, no need to pseudonymize data. If explants are used, data will be already pseudonymized by clinical partners.
REHAZENTER	Employing a pseudonymization process, each patient is allocated a distinctive identifier logged in a correspondence table. This table, necessary for reidentifying individuals, remains exclusively accessible to one researcher, safeguarded within a restricted-access folder in the Rehazenter's information system, protected by a password.
CorTec GmbH	No access to patient data.

Table 8 Process to protect and pseudonymize data

All AI-Hand project partners involved in generating or collecting data for the project are responsible for a secure recovery, storage, and transfer of data - both personal and non-personal data included. The project coordination team supports partners with specific information about procedures and general regulation if needed.

The Consortium Agreement rules the access rights for implementation and exploitation of the results of the project including data management. Specific responsibilities regarding data are described in the section 4.4 of the AI-Hand Consortium Agreement, currently under signature. As part of the project's implementation, the partners agreed on their individual liability in processing personal data in accordance with their distributive role in the project (as described in the Annex 1 of the Grant Agreement). The partners also agreed on cooperating and complying with applicable regulation and legislation, notably Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 (GDPR) to ensure the compliance of personal data processing operations conducted as part of the project.

The parties thus reciprocally undertake as follows:

1. To process personal data collected though the project only to the extend and for the purposes set for the implementation of the project.
2. To ensure the security and confidentiality of personal data, implementing appropriate technical and organisational measures, in particular to prevent it from being distorted, damaged or communicated to third parties outside the framework of the collaboration subject of the CA.
   The measures taken by the partners take into account the most recent technical possibilities and the cost of their implementation, the characteristics of the processing (nature, scope, purpose) and the risks presented for the rights of the data subjects.

3. To duly inform data subjects about the processing of their personal data, and set up a prior consent procedure when required;
4. To sign appropriate clauses and take appropriate measures to safeguard the rights of the individuals in case they hire a third party to process personal data or operate a transfer outside of the European Economic Area;
5. To cooperate at all times and in all transparency to facilitate compliance to personal data regulation, especially in case of data subjects right request and of personal data breach;

The scope of the Parties collaboration extends to all the steps and procedures necessary for monitoring and maintaining the Project's compliance with GDPR, in particular:

- The fair and transparent information of data subjects, as well as the management of requests to exercise their rights and, where appropriate, the collection of their consent;
- The notification of personal data violations to the competent authorities and their possible communication to data subjects within the time limits prescribed by the regulations;
- Carrying out data protection impact assessments in the event of processing operations generating a high risk for data subjects and, where appropriate, prior consultation of the competent supervisory authority;
- The formalisation and provision of any documentation useful for demonstrating the conformity of the processing operations implemented, particularly where there is a request or supervision by the public authorities responsible for the protection of personal data.

6. To comply with any other applicable local regulation and legislation when required by their assigned activities.

The Parties shall therefore each bear the legal risks relating to the processing of personal data, as far as they are concerned.

The Annex 5 “Protection of personal data” of the CA defines the conditions in which the joint controllers undertake to carry out the Processing operations defined hereafter under the Contract to which it applies. The Annex is attached to this DMP as Annex 1.

As soon as the publication targets are achieved, the public collected datasets will be deposited as previously described. More precisely, open data security will be addressed by taking advantage of Research Data Gouv of secure storage, backup and preservation and protected transfer mechanisms. Regarding the collected data tied to the confidential datasets, different approaches will be used by each data-owner’s organisation, but common rules apply. As presented in Table 1, data will be saved in servers and under the direct control and management of the organisation’s personnel. Such infrastructure is equipped with different features, e.g., secure physical access, air conditioning, fire protection measures, and hardware/electricity recovery measures.

Different data access permissions, e.g., read-only, read-write, etc., will be granted to users and authorised computers by relevant staff, according to a well-defined protocol. Additionally, confidentiality is guaranteed by supplementary methods, e.g., encryption and pseudonymisation, depending on the data’s nature and applications. Furthermore, regular backups are envisaged for either security purposes, hardware failure recovery, or for archival purposes. Following the completion of the project, all the

responsibilities concerning data recovery and secure storage will go to the repository storing the dataset. Long-term preservation is guaranteed even in the unlikely event that Research Data Gouv will cease operation; migration of content on other repositories is planned.

VI. ETHICS

Two preclinical studies with pigs and three clinical investigations will be conducted and require agreement on national ethics committees in France and in Luxembourg, and Health Agencies (NCA) for the First in Man clinical investigation only. In addition, the Operational Committee for the Evaluation of Legal and Ethical Risks (COERLE) of INRIA will be consulted for the protocol design. The COERLE is an INRIA body responsible for advising on ethical and legal issues arising in the context of research activities and for supporting research teams in addressing these issues. It is composed of scientists from different backgrounds and cultures, both internal and external, legal experts, and specialists in data protection and security. This Committee helps teams to secure their research from an ethical and legal standpoint and to improve and refine their experimental approach. Far from acting as a censor or arbiter of ethical elegance, it contributes in a positive and benevolent spirit to ensuring that INRIA's research is conducted within an ethically responsible framework.

The following international standards will be followed:

- Declaration of Helsinki
- MDR 2017/745
- Good Clinical Practice ISO 14155.2020
- National specific rules in France and Luxembourg

Patients will be volunteers and clinical trials will be conducted with fully informed consent, and explained benefit risk analysis based on ISO14971.

Animal experimentations will be subject to the dedicated ethics committees for approval. They are dedicated to the Biological Risk Assessment (BRA) of the AIMD that is mandatory prior to a clinical use. It will be carried out in particular to fulfil the ISO 10093-1 and the next relevant standard. Two INRIA team members have the agreements to design animal studies and perform animal surgery.

Experimentation on dead human corpse will be subject to ethics committees for approval. They are conducted by surgical team, with assistance from Neurinnov and INRIA team members. The aim of these trials is to determine the parameters of the surgical operation dedicated to the implantation of the AIMD.

ANNEX 1 Description of clinical trials

Horizon Europe Essential Information for Clinical Studies in Horizon Europe

Version 1.1- 8 April 2021

Three clinical trials are envisioned with AI-HAND project, preliminary description is given in the following.

First In Man trial-AI-HAND-FIM

1. Description of the clinical study

As the Clinical trial is scheduled in about 2 years, all details are not yet available. It will be precisely reported in due deliverables of WP6.

1.1. Title, acronym, unique identifier (e.g., EudraCT Number, or identifier from ISCRTN, ClinicalTrials.gov if available) of the clinical study

Title: First-in-man trial of an implanted device to restore Hand function in person with complete high tetraplegia.

Acronym: AI-HAND FIM

Clinical Trial registration will be performed at the same time as the protocol submission to the National Ethics Committee and Health Agencies.

1.2. Study rationale

Please provide the overall rationale for conducting the proposed study.

In people with high tetraplegia (neurological level C5 or above), functional electrical stimulation is currently the only approach that enables considering functional restoration of grasping in the case where the active muscles resources below the elbows are absent or insufficient to allow tendon or nerve transfer surgery. To date, no solution has emerged to meet the expectations of patients with high tetraplegia who are completely dependent on a third party.

1.2.1. Extent and evaluation of current knowledge directly linked to the scientific question(s) to be answered by the clinical study.

Like the first implanted electrical stimulation neuroprosthesis, Freehand™ (Neurocontrol, Cleveland, USA), the vast majority of devices using FES are directly stimulating sub lesional muscles that have retained their innervation and contractibility (surface, intramuscular or epimysial electrodes). These approaches are requiring a high number of internal components as each single muscle must be activated via a dedicated electrode (12 electrodes for the FreeHand and 36 in a more recent experiment). Retrospective studies demonstrated good patient compliance with the Freehand system and functional usefulness. Unlike muscle (epimysial) stimulation, direct neural stimulation enables, with a single electrode, to stimulate several muscles that are difficult to reach due to their proximity to each other and/or their depth. Besides, it requires less energy, considerably limiting the number of implanted elements and drastically reducing the risk of complications.

1.2.1.1. Outcomes (efficacy, safety) of completed and number of ongoing clinical studies utilizing the same intervention in the same indication (including review of public registers)

Since Freehand marketing is discontinued, no solution has emerged to meet the expectations of patients with high tetraplegia and no motor control of their upper limbs. This is a First-in-man CT so there is no other CT utilizing the same surgical approach, the same stimulation paradigms (multi-contact, fascicular electrical stimulation), the same device and the same indications.

1.2.1.2. Level of evidence related to the mechanism of action of the intervention in the planned clinical study population.

The promise of a neural approach to electrically stimulate the hand was validated in a 1st feasibility study (AGILIS Project No. RCB 2014-A01752-45/1) with 9 tetraplegic patients. The procedure consisted of placing a multi contact "cuff electrode" around the radial or the median nerve and observing the effects of neural electrical stimulation in terms of muscle selectivity, force produced, and movement induced. This procedure was applied intraoperatively in tetraplegic subjects undergoing tendon surgery to restore active extension of the elbow, with an open approach allowing direct access to either the radial or the median nerve, depending on the subject. The electrodes were tested intraoperatively and removed immediately after testing. In other words, they were left in place for 30 to 45 minutes. The summary of the results of this first study (Tigra et al J Neuro Engineering Rehabil 17, 66 (2020) is:

- No report of adverse effects.
- No electrode or stimulator failures were noted.

For all subjects, it was possible to selectively stimulate groups of muscle to obtain thumb and finger opening, or thumb and finger flexion, and to obtain possibly functional grasping such as pinch with thumb opposition or palmar grip.

These trials were performed under general anesthesia and only one nerve was stimulated for each patient. A second feasibility study (Project No. RCB 2016-A00711-50) with 17 tetraplegic patients focused on the subjects' ability to use voluntary contractions of supra-lesional muscles (EMG recordings in 8 subjects) or voluntary shoulder movements (inertial recordings in 9 subjects) to either drive the movements of a robotic hand or to trigger surface electrical stimulation of forearm muscles. All patients mastered the proposed interface after a short familiarization time (Tigra et al., 2018).

A 3rd preliminary study (Project No. RCB 2019-A02037-50) with 2 tetraplegic patients -neurological level C4, AIS A -consisted of the percutaneous implantation of both aforementioned cuff electrodes: one around the median nerve and the other around the radial nerve. They were left in place for 28 days to comply with the European Medical Device Regulation 17/745. The purpose of the study was to suggest, over a credible time frame, both the safety and the ability of multi contact electrodes to produce and synergistically combine movements for useful grasps. The success rate in performing prehension tasks on the motor ability scale over what was considered a short duration was 54% for one individual and 51% for the other. Command compliance was >90% for the patient who opted for the inertial units and 100% for the patient who chose EMG sensors. The stimulation configurations all proved selective. The safety of the procedure was demonstrated under close supervision. This follow-up allowed for the perfect control, under antibiotic therapy, of a local superinfection point around the emergence of a cable in 1 of the 2 participants (Fattal et al. J of Neurotrauma 2022).

1.3. Objective(s) of the clinical study

Please differentiate between primary and secondary objective(s)

- The CT primary objectives are:

i)To improve patients' perceived performances in prioritized activities. The Canadian Occupational Performance Measure (COPM), a patient-centered approach will be used. It is designed to detect a person's self-perception of activity performance over time.

ii)To improve patients' perception of Personal Wellbeing. The Personal Wellbeing Index -Adult (PWI-A) will be used. There are eight items in the adult PWI scale, each one corresponding to a quality-of-life domain as: standard of living, health, life achievement, personal relationships, personal safety, community-connectedness, future security.

- The CT secondary objectives are:

i)To study the safety of the surgical & experimental procedures and the ability of electrodes to induce synergistic motor activations leading to functional movements,

ii)To assess different modalities for controlling electrical stimulation of the hand (IMU, EMG, Voice)

1.4. Characteristics of the study population (size, age group, sex distribution inclusion and exclusion criteria; all items with justification!)

- Inclusion criteria: age between 18 and 65, tetraplegia with a single neurological level ≥ C6, AIS A or B, neurological stability (no change in motor testing for the last 6 months), non-eligibility for tendon transfer surgery, group 0, 1 or 2 (ICSHT classification).
- Exclusion criteria: unstable seizure, pacemaker, dermatological problems contraindicating the application of surface electrodes and an electrical mapping identified as negative at the inclusion visit, i.e., with muscles rated < 4/5 MRC (Medical Research Council).

1.4.1. Details on sample size and power calculation

3 patients per clinical center

1.5. Design of the clinical study (controlled / uncontrolled; randomized; open / blinded; parallel group / cross over / other; please justify the appropriateness of the selected design)

The CT is a prospective exploratory, non-controlled study as it relates to a proof-of-concept first-in-man CT.

1.6. Type of intervention (medicinal product / advanced therapy medicinal product / medical device / in vitro diagnostic medical device / surgical or other invasive procedure / other medical intervention, including, e.g., counselling)

The investigation is about an Active Implantable Medical Device (class III) leading to a surgical procedure to implant 2 epineural electrodes on the radial and median nerves, and an Implanted Pulse Generator connected to these 2 electrodes. Energy and data are provided through a wireless link so that no percutaneous lead is present, the system is fully implanted with an external control unit.

1.7. Description and timing of study procedures

Please provide an overview, preferably in a tabular format, about the schedule of study procedures. Please give a simple statement on how long individual patients or healthy volunteers participate in the clinical study.

The device is implanted for a long-term study (>30 days). After implantation, the patient will stay during a month in a clinical context for tuning, training and full assessment, and then will be back home with a monthly follow-up during the first year, then a yearly follow-up in accordance with MDR 2017/745 regulation.

2. Preparedness status

2.1. Development of the clinical protocol

Please describe how the below aspects have been or will be addressed in developing the clinical study protocol (if applicable):

2.1.1. Scientific advice from regulatory and health technology assessment bodies

The CT concerns a class II device without CE marking in two EU countries (Luxembourg/France). Both beneficiaries will apply to ethics committees together with national health competent authorities following MDR 2017/745 regulation. (In France CPP, Comité de Protection de Personnes, and ANSM, Agence Nationale de la sécurité du médicament)

2.1.2. Clinical efficacy, safety, and methodological guidelines (including guidelines on statistics)

Among many the most important norms we will comply with are ISO 14155 Good clinical practice, ISO 14971 risk analysis, ISO 10993-1 Biological risk assessment, and the MDCG guidance's.

2.1.3. Involvement of citizens / patients, careers in drawing up the clinical study protocol

The CT is based on complex technology. Patients, Medical Doctors and caregivers were questioned before starting this research in order to set the unmet clinical needs and thus the expected clinical benefit (the main objective of the study). Technical performances and safety assessments are based on state-of-the-art and specific assessments that will be carried out during the project by manufacturers (secondary objective of the study)

2.2. Regulatory intelligence to ensure timely regulatory approval and ethics clearance of the clinical study in all jurisdictions where its implementation is planned.

Please provide information on the following regulatory and ethics aspects:

2.2.1. How the consortium will ensure access to regulatory expertise necessary to get advice on, and management of, regulatory affairs activities in all concerned jurisdictions?

The consortium has the experience of such protocols as beneficiaries already acted as promoter/investigator/manufacturer (USSAP, INRIA, NEURINNOV) and thus endorsed the role of CRO. However, as the researchers go through a full implanted, long term, class III device they will be supported by ICARE Laboratory (Biological Risk Assessment) and EFOR (CRO). Even though we do not aim at CE marking within the project we also have support from BSI notified body.

2.2.2. How the consortium will ensure access to ethics expertise necessary to get advice on current proceedings and documentation requirements of all concerned ethics committees?

INRIA (COERLE committee), USSAP, Rehazenter and manufacturer already provided successful support to Investigation Brochure documentation in previous ethics committee/Health Agency applications for which they obtained full clearance (with invasive technology)

2.3. How the scientific and operational governance of the clinical study will be ensured?

2.3.1. Please give details about the sponsor(s) (name, type of entity, seat or country of residence).

- USSAP (partner 5), Rehabilitation center, Perpignan, France
- Rehazenter (partner 3), Rehabilitation center, Luxembourg

2.3.2. Please describe the composition, the role and the functioning of the planned board(s), governing bodies.

To be defined but an independent scientific board will be set to follow the CT. A board composed of at least one Medical Doctor and one researcher of the domain.

3. Operational feasibility

3.1. Please describe how the availability of the intervention(s) (including comparators) is secured throughout the entire implementation phase (give details on manufacturing, packaging / labelling operations, storage, logistical, import/export issues, etc.)

There is no comparators and the device provision and manufacturing is the core of the project and will be delivered by NEURINNOV (partner 2) and CorTec GmbH (partner 4)

3.2. Please describe how the study population will be recruited.

Please give details on the recruitment strategy, monitoring of progress and potential mitigation measures

Both the Rehazenter and the USSAP-CBV centers are recognized for their expertise in the care of spinal cord injury patients. Their numerous publications dedicated to spinal cord injuries attest this. Both have the potential of recruiting 3 patients each. This is the goal of the CT. No advertising will be necessary.

3.2.1. How many clinical sites will contribute to the recruitment of the study population in which countries? Are these clinical sites part of an established clinical trial network? Please also describe the selection criteria of the clinical sites.

Two, Luxembourg, France. The selection criterion for such a complex device and CT is i) centers specialized in the care of the targeted population, ii) centers that have experience in implanted medical devices, iii) centers who know each other, iv) experienced surgeons who have already implanted epineural electrodes.

3.2.2. Will recruitment of the study population be of competitive nature between the clinical sites? (Please describe how under performance of individual clinical sites in recruitment will be managed.)

No. On the contrary each center could provide more than 3 patients; they agree to limit to 3 and benefit from each other to get knowledge with cross experience as the approach is totally new.

3.2.3. What evidence supports the ability of the individual clinical sites to recruit the required number of study participants within the planned timeline (e.g., documented performance in previous clinical studies of similar complexity targeting very similar study population)?

During the COVID crisis, in a very short period of time (2 months) USSAP succeeded in recruiting 2 patients with tetraplegia for a previous protocol so 3 patients over a year with an even more beneficial protocol for the patient should not rise any problem (see data above). Both the Rehazenter and the USSAP-CBV centers are recognized for their expertise in the care of spinal cord injury patients. The numerous publications dedicated to spinal cord injuries attest this.

3.3. Please describe what additional supply (e.g., an electronic device for remote data capture, a specific instrument for administering the investigational product, etc.) is necessary to carry out the required study procedures and how this supply will be made available to the clinical sites.

Manufacturers will provide the device and all necessary accessories to each center.

3.4. Please provide plans on data management aspects (data standards, type of data capture, verification of data, central data collection, cleaning, analysis, reporting, security)

Secured server will be set to process non personal data. Personal data won't be shared and will be stored by clinical partners only for tracing and survey purposes only. GPRD compliance will be ensured, and no data will be disclosed. Only anonymous processed data for the needs of scientific publications will be publicly available.

3.5. Please give details on how reporting obligations (regarding study initiation, safety of study participants, ethical concerns, quality issues, integrity of data, study results) to regulatory bodies and ethics committees will be met.

The consortium follows the national regulations and EU regulations that fully comply with all these issues.

3.6. Please list all items of the sponsor's responsibilities (e.g., monitoring clinical sites, meeting regulatory obligations, data management, etc.) that will be supported by entities that are not part of the sponsor's organization. Please describe how the sponsor will ensure oversight of these activities.

Monitoring clinical site, meeting regulations obligations & apply for ethics and safety committees' clearance, Serious Side Effects reporting, insurances, patient recruitment.

3.7. What are the plans for major study milestones and what evidence supports its feasibility?

Please describe a realistic plan (based on prior experience) detailing the time necessary for (i) compiling the required regulatory and ethics submission package, (ii) receipt of regulatory and ethics approval, (iii) initiation of clinical site(s), (iv) completion of recruitment of the study population, (v) final assessment of all study participants, (vi) analysis and reporting of the study results.

- Safety qualifications & Biological Risk Assessment: 1year
- Ethics committee and National Health Agency documentation preparation: 3 months
- Ethics committee / National Health Agency application clearance: 4 to 6 months
- Patients' recruitment & completion of the research part: 12 months (continuous recruitment)
- Protocol duration: 1 month (in the clinic post-operative)
- Patients' follow-up at home: 1 year(monthly) and then yearly mandatory control.

Non-invasive Clinical trial - FORCE-CONTROLED GRASP -AI-HAND-CT1

1. Description of the clinical study

Clinical trials are envisioned with participants before actual FIM (WP5). All details are not yet available.

1.1. Title, acronym, unique identifier (e.g., EudraCT Number, or identifier from ISCRTN, ClinicalTrials.govif available) of the clinical study

Title: Feasibility study on force -controlled grasp based on biofeedback.

Acronym: AI-HAND-CT1

Clinical Trial registration will be performed at the same time as the protocol submission to the French National Ethics Committee (CPP) and Health Agency (ANSM).

1.2. Study rationale

Please provide the overall rationale for conducting the proposed study.

Future users of the implanted neuroprosthesis should be able to modulate the force applied during grasping in order to adapt to different objects and to compensate for fatigue or low quality of grasping gesture. We hypothesize that an adapted biofeedback along with a closed-loop control law of the AIMD will allow the users to pilot the strength of the grip.

1.2.1. Extent and evaluation of current knowledge directly linked to the scientific question(s) to be answered by the clinical study.

In previous work we developed a 1st control interface allowing the user to select pre-programmed stimulation patterns based on voluntary movements from muscles above the spinal cord lesion. This approach lacks flexibility to adapt grasping strength to hold objects of different weights or to compensate for muscular fatigue. To do so, the user of the device should be able to intuitively adjust the targeted grasp strength over time, depending on the object to be held and on the quality of the obtained grasp, evaluated thanks to relevant biofeedback signals (visual, audio, etc.). We will investigate how to inform the user on the quality of the obtained grasp, by providing feedback on fingers positioning around the object and/or on the force applied by each finger. This requires instrumenting the hand/object interface and setting up communication pathways: providing feedback information to the user and controller and collecting targeted grasping intentions from the user. In that way, the stimulation current intensity will be low-level modulated in closed-loop while being higher-level tuned by the user. This closed-loop control scheme will be investigated and tested in preliminary experiments with healthy and tetraplegic participants. It will represent an opportunity to explore a wide range of piloting interfaces using existing sensors (microphone, IMU, EMG, etc.) to evaluate their usability and the quality of their output signals. Once the proof of concept has been validated with external stimulation in dedicated clinical trials, it will be tested in the participants of the FIM.

1.2.1.1. Outcomes (efficacy, safety) of completed and number of ongoing clinical studies utilising the same intervention in the same indication (including review of public registers)

Based on previous studies we will investigate different biofeedback modalities and assess their usability for participants with complete tetraplegia.

We will also validate a Human Man Interface (HMI) allowing the user to pilot the grip strength based on this biofeedback. We will take care of carrying an extended state of the art on the topic.

1.2.1.2. Level of evidence related to the mechanism of action of the intervention in the planned clinical study population.

This clinical study will allow us to optimize the tools that will be integrated in the FIM (controller, interface, biofeedback)

1.3. Objective(s) of the clinical study

Please differentiate between primary and secondary objective(s)

- Primary objective: to validate a controller piloted by the user to modulate the force applied to objects by the stimulated hand.
- Secondary objectives: to assess the usability of different biofeedback modalities designed to inform the user of the neuroprosthesis about the force applied to an object and the positioning of the fingers around the object.

1.4. Characteristics of the study population (size, age group, sex distribution inclusion and exclusion criteria; all items with justification!)

- Inclusion criteria: age between 18 and 65, tetraplegia with a single neurological level ≥ C6, AIS A or B, neurological stability (no change in motor testing for the last 6 months), non-eligibility for tendon transfer surgery, group 0, 1 or 2 (ICSHT classification).
- Exclusion criteria: unstable seizure, pacemaker, dermatological problems contraindicating the application of surface electrodes and an electrical mapping identified as negative at the inclusion visit, i.e., with muscles rated < 4/5 MRC (Medical Research Council).

1.4.1. Details on sample size and power calculation

Feasibility study -10 subjects

1.5. Design of the clinical study (controlled / uncontrolled; randomized; open / blinded; parallel group / cross over / other; please justify the appropriateness of the selected design)

The CT is a prospective exploratory, non-controlled study as it relates to a feasibility study.

1.6. Type of intervention (medicinal product / advanced therapy medicinal product / medical device / in vitro diagnostic medical device / surgical or other invasive procedure / other medical intervention, including, e.g., counselling)

Non-invasive procedure.

1.7. Description and timing of study procedures

Please provide an overview, preferably in a tabular format, about the schedule of study procedures. Please give a simple statement on how long individual patients or healthy volunteers participate in the clinical study.

The protocol will be described precisely over the 1st year. Each subject will participate into several sessions to evaluate the usability of different biofeedback (vibration, audio, visual) using dedicated scales such as the System Usability Scale (SUS). The chosen biofeedback will be used in a last session to assess the feasibility for the user to control grip strength on a software support and on external FES (CE marked) applied via skin electrodes.

2. Preparedness status

2.1. Development of the clinical study protocol

Please describe how the below aspects have been or will be addressed in developing the clinical study protocol (if applicable):

2.1.1. Scientific advice from regulatory and health technology assessment bodies.

2.1.2. Clinical efficacy, safety, and methodological guidelines (including guidelines on statistics)

2.1.3. Involvement of citizens / patients, carers in drawing up the clinical study protocol

During the protocol (before FIM), patients will regularly give their feedback, based on surveys, on the interface. This will be part of the information -along with other considerations related to the quality of the signals-that will help us determine which biofeedback and control law are the most suited for this application.

2.1.4. Regulatory intelligence to ensure timely regulatory approval and ethics clearance of the clinical study in all jurisdictions where its implementation is planned. Please provide information on the following regulatory and ethics aspects:

2.1.5. How the consortium will ensure access to regulatory expertise necessary to get advice on, and management of, regulatory affairs activities in all concerned jurisdictions?

The consortium has the experience of such protocol as partners already acted as promoter/investigator/manufacturer (USSAP, INRIA, NEURINNOV) and thus endorsed the role of CRO.

2.1.6. How the consortium will ensure access to ethics expertise necessary to get advice on current proceedings and documentation requirements of all concerned ethics committees

INRIA (COERLE ethics committee) and USSAP have many years of experience in designing clinical protocols and applying to national ethics committee.

2.2. How the scientific and operational governance of the clinical study will be ensured?

2.2.1. Please give details about the sponsor(s) (name, type of entity, seat or country of residence).

USSAP (partner 5) Rehabilitation center, Perpignan France.

Since 2021, USSAP has become a single nonprofit association through a process of bringing together and merging 4 associations.

2.2.2. Please describe the composition, the role and the functioning of the planned board(s), governing bodies.

3. Operational feasibility

3.1. Please describe how the availability of the intervention(s) (including comparators) is secured throughout the entire implementation phase (give details on manufacturing, packaging / labelling operations, storage, logistical, import/export issues, etc.)

3.2. Please describe how the study population will be recruited

Please give details on the recruitment strategy, monitoring of progress and potential mitigation measures

USSAP has the potential to recruit 10 patients. The institution includes a spinal cord injury unit. No advertising will be necessary. The medical data registers will be consulted. A pre-selection will be made on the basis of inclusion and non-inclusion criteria.

3.2.1. How many clinical sites will contribute to the recruitment of the study population in which countries? Are these clinical sites part of an established clinical trial network? Please also describe the selection criteria of the clinical sites.

Only USSAP

3.2.2. Will recruitment of the study population be of competitive nature between the clinical sites? (Please describe how underperformance of individual clinical sites in recruitment will be managed.)

No.

3.2.3. What evidence supports the ability of the individual clinical sites to recruit the required number of study participants within the planned timeline (e.g., documented performance in previous clinical studies of similar complexity targeting very similar study population)?

The institution includes a spinal cord injury unit. The USSAP-CBV centers is recognized for its expertise in the care of spinal cord injury patients. The numerous publications dedicated to spinal cord injuries attest this.

3.3. Please describe what additional supply (e.g., an electronic device for remote data capture, a specific instrument for administering the investigational product, etc.) is necessary to carry out the required study procedures and how this supply will be made available to the clinical sites.

Classical devices used for motion analysis will be used and are available at INRIA (infrared motion capture, leap motion, video cameras, force gauges...). We will equip ourselves with power grip and finger force sensors, which provide biomechanical quantities that are part of the biofeedback we wish to investigate.

3.4. Please provide plans on data management aspects (data standards, type of data capture, verification of data, central data collection, cleaning, analysis, reporting, security)

Secured server will be set to process non personal data. Personal data won't be shared and will be stored by clinical partners only for tracing and survey purposes only. GPRD compliance will be ensured, and no data will be disclosed. Only pseudonymous processed data for the needs of scientific publications will be publicly available. A risk analysis will be carried by INRIA for data security.

3.5. Please give details on how reporting obligations (regarding study initiation, safety of study participants, ethical concerns, quality issues, integrity of data, study results) to regulatory bodies and ethics committees will be met.

The consortium follows the national regulations and EU regulations that fully comply with all these issues.

3.6. Please list all items of the sponsor's responsibilities (e.g., monitoring clinical sites, meeting regulatory obligations, data management, etc.) that will be supported by entities that are not part of the sponsor's organization. Please describe how the sponsor will ensure oversight of these activities.

Monitoring clinical site, meeting regulations obligations & apply for ethics and safety committees' clearance, Serious Side Effects reporting, insurances, patient recruitment.

3.7. What are the plans for major study milestones and what evidence supports its feasibility? Please describe a realistic plan (based on prior experience) detailing the time necessary for (i) compiling the required regulatory and ethics submission package, (ii) receipt of regulatory and ethics approval, (iii) initiation of clinical site(s), (iv) completion of recruitment of the study population, (v) final assessment of all study participants, (vi) analysis and reporting of the study results.

- Ethics committee and National Health Agency documentation preparation: 3 months
- Ethics committee / National Health Agency application clearance: 4 to 6 months
- Patients' recruitment & completion of the research part: 12 months
- Protocol duration: 1 month

Non-invasive Clinical trial - Identification of parameters and validation of HANDSIMULATOR -AI-HAND-CT2

1. Description of the clinical study

Clinical trials are envisioned with participants before actual FIM (WP5). All details are not yet available.

1.1. Title, acronym, unique identifier (e.g. EudraCT Number, or identifier from ISCRTN, ClinicalTrials.gov if available) of the clinical study

Validation of numerical neuro-musculoskeletal models developed in simulation via experimental data collection.

Title: Identification of parameters and validation of Hand Simulator

Acronym: AI-HAND-CT2

Clinical Trial registration will be performed at the same time as the protocol submission to the French National Ethics Committee (CPP) and Health Agency (ANSM).

1.2. Study rationale

Please provide the overall rationale for conducting the proposed study.

The development of a simulation software is motivated by the complexity of choosing electrical stimulation patterns, the difficulty of predicting their functional effect on the body and the specific anatomy of each patient. To calibrate and validate our numerical models, we need to conduct experiments on real patients in order to compare experimental data to simulated ones and assess the validity of our software.

1.2.1. Extent and evaluation of current knowledge directly linked to the scientific question(s) to be answered by the clinical study

Choosing stimulation patterns is challenged by the size of search space (3D currents, large number of parameters), the difficulty to predict their functional effects on musculoskeletal system (motion kinematics and dynamics) and the specific anatomy of each patient. Hand is a particularly complex part of the body to model and it is difficult to objectively assess the quality of its interaction with external objects to grasp. In view of this complexity, we will develop a software that will simulate the upper limb, from electrical stimulation up to the resulting motion, while being patient-specific. It will be made compatible with out-of-the-shelf optimization software that will allow to predict optimized stimulation patterns (for instance, from functional, power consumption or fatigue point of views). The optimized solution will be preliminary tested with healthy participants and participants with complete tetraplegia (using external electrical stimulation) in a dedicated clinical trial before being tested with the participants of the FIM. This reliable simulation tool will also allow us to infer biomechanical quantities (range of motion, muscle forces, joint torques, etc.) from experimental data of the clinical trials, without burdening the protocols and in real-time, which represents a crucial feature for the operator to tune the stimulator. Thanks to its real-time capabilities, it will most probably also play a role in the feedback flow provided to the patient.

1.2.1.1. Outcomes (efficacy, safety) of completed and number of ongoing clinical studies utilising the same intervention in the same indication (including review of public registers)

Based on previous studies we will investigate different biofeedback modalities and assess their usability for participants with complete tetraplegia. The consortium also validates a Human Man Interface (HMI) allowing the user to pilot the grip strength based on these bio feedback.

1.2.1.2. Level of evidence related to the mechanism of action of the intervention in the planned clinical study population.

This clinical study will allow us to validate the hand simulator with experimental data.

Objective(s) of the clinical study

Please differentiate between primary and secondary objective(s)

- Primary objective: To compare experimental and simulated data of evoked hand motion, to validate the hand simulator.
- Secondary objective: To optimize clinical interface.

1.3. Characteristics of the study population (size, age group, sex distribution inclusion and exclusion criteria; all items with justification!)

Inclusion criteria: age between 18 and 65, tetraplegia with a single neurological level $\geqslant$ C6, AIS A or B, neurological stability (no change in motor testing for the last 6 months), non-eligibility for tendon transfer surgery, group 0, 1 or 2 (ICSHT classification).

Exclusion criteria: unstable seizure, pacemaker, dermatological problems contraindicating the application of surface electrodes and an electrical mapping identified as negative at the inclusion visit, i.e., with muscles rated < 4/5 MRC (Medical Research Council).

1.3.1. Details on sample size and power calculation

Feasibility study -10 subjects

1.4. Design of the clinical study (controlled / uncontrolled; randomised; open / blinded; parallel group / cross over / other; please justify the appropriateness of the selected design)

The CT (Clinical Trial) is a prospective exploratory, non-controlled study as it relates to a feasibility study.

1.5. Type of intervention (medicinal product / advanced therapy medicinal product / medical device / in vitro diagnostic medical device / surgical or other invasive procedure / other medical intervention, including, e.g., counselling)

Non-invasive procedure.

1.6. Description and timing of study procedures

Please provide an overview, preferably in a tabular format, about the schedule of study procedures. Please give a simple statement on how long individual patients or healthy volunteers participate in the clinical study.

The protocol will be described precisely over the 2nd year. Each subject will participate into several sessions to record several characteristic motions we are interested in for the FIM (hand grasps and openings).

2. Preparedness status

2.1. Development of the clinical study protocol

2.1.1. Scientific advice from regulatory and health technology assessment bodies

2.1.2. Clinical efficacy, safety, and methodological guidelines (including guidelines on statistics)

2.1.3. Involvement of citizens / patients, careers in drawing up the clinical study protocol

2.2. Regulatory intelligence to ensure timely regulatory approval and ethics clearance of the clinical study in all jurisdictions where its implementation is planned.

Please provide information on the following regulatory and ethics aspects:

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Only USSAP-Center Bouffard-Vercelli

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No.

3.2.3. What evidence supports the ability of the individual clinical sites to recruit the required number of study participants within the planned timeline (e.g., documented performance in previous clinical studies of similar complexity targeting very similar study population)?

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3.3. Please describe what additional supply (e.g., an electronic device for remote data capture, a specific instrument for administering the investigational product, etc.) is necessary to carry out the required study procedures and how this supply will be made available to the clinical sites

Classical devices used for movement reconstruction will be used and are available at INRIA (MOCAP, leap motion, video cameras, force jauges...). The consortium is equipped with force sensors.

3.4. Please provide plans on data management aspects (data standards, type of data capture, verification of data, central data collection, cleaning, analysis, reporting, security)

Secured server will be set to process non personal data. Personal data won't be shared and will be stored by clinical partners only for tracing and survey purposes only. GPRD compliance will be ensured, and no

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