**RESEARCH PROPOSAL MASTER MEDICINE**

Title internship: Improvement in ambulatory function through addition of Functional Electric Stimulation (FES) in patients with Spinal Cord Injury (SCI) utilising Brain-Spine Interface (BSI)

Voor- en achternaam student: Mel Visscher  
 **Host internship**Name institute: École Polytechnique Fédérale de Lausanne (EPFL)  
Department: Life sciences (laboratory UpCourtine)  
City: Lausanne  
Country: switzerland  
Daily supervisor: Henri Lorach  
Internal supervisor\*: Ilse van Nes

\* Note: Compulsory. The internal supervisor has to have a PhD degree and an affiliation at the Radboudumc

**Date and length**Start date internship: 28-10-2024  
End date internship: 31-01-2024

*Extended internship?* No, 12 weeks  
 16 weeks  
 20 weeks  
 24 weeks

Motivation for extension

N/A

**Type of internship**Titel stage: Improvement in ambulatory function through addition of Functional Electric Stimulation (FES) in patients with Spinal Cord Injury (SCI) utilising Brain-Spine Interface (BSI)  
Title (English): Improvement in ambulatory function through addition of Functional Electric Stimulation (BSI) in patients with Spinal Cord Injury (SCI) utilising Brain-Spine Interface (BSI)

Nature of the research (Remark: My supervisor decided on qualitative as a correction of the “quantitative” box which I checked. I suspect he did so because this study won’t achieve statistical significance. I agree with you that quantitative is a more sensible category.) Quantitative  
 Qualitative  
 Laboratory or fundamental   
 Systematic review +  meta analyse\*  
\* systematic review (met meta analyse) wordt ontraden i.v.m. ontbreken van onderwijs hierover in het curriculum

Discipline (e.g. pediatrics): PMR (Physical Medicine & Rehabilitation) and biomedical engineering

Material / data Existing material  
 Collect material by yourself

*WMO* Study is not subject to WMO (NB: Swiss regulatory approval is obtained)  
 Study is subject to WMO and CMO approval is present\*  
 CMO approval has been requested  
\* Subject to WMO research: approval is required when submitting the internship proposal

*Activities* Recruitment / inclusion of participants  
 Data collection from participants (e.g. administering a questionnaire)  
 Measurements of (bio)material   
 Conducting interviews (qualitative research: semi-structured interviews, focus group etc.)  
 Coding interviews (qualitative research)  
 Learning specific (lab) skills   
 Following outpatient clinics / operations with regard to internship subject  
 Preparation of CMO application  
 Working with (part of) an existing data file  
 Compile the data file yourself  
 Simple statistical analyses (descriptive statistics, T-test etc.)  
 Advanced statistical analyses with the help of a statistician (e.g. multivariable analysis, etc.)

**Personal learning objectives**1st Learning objective

Get acquainted with working with a BCI (Brain-computer interface), both in terms of practical in-person application with research subjects and in terms of the underlying software

2nd Learning objective

Get acquainted with working with an Functional Electric Stimulation (FES) system, specifically in conjunction with a Brain-Computer Interface (BCI).

3rd Learning objective (optional)

Get experience in writing a scientific article and generally working on the intersection of engineering and medicine.

**Project outline**

(see also steps and tips on Brightspace)

**Background and goal of the study**

The ability to walk is one of most important functions to ensure personal autonomy and social inclusion. (De Rooij, I.J.M. et al., 2021) While the various aetiologies are legion, the singular impact on Quality of Life and autonomy in Activities of Daily Living (ADL) is undeniable. (Jaewon, M. et al., 2023)

Various high-tech solutions such as exoskeletons have been attempted in order to give tetra- or paraplegics their ability to walk back. Many of these solutions however, have their drawbacks as they are often insufficient to use in daily life, at least in part because of the use of preprogrammed walk cycles or the requirement of residual muscle function. (Rodríguez-Fernández, A. et al., 2021)

The Swiss laboratory UpCourtine has developed a solution where a Brain-Spine Interface (BSI) is established. (Lorach, H. et al., 2023) While this solution has demonstrated an immediate impact on walking ability, the recovery thereof is incomplete.

The present study will attempt to utilise the same information generated by the brain implant or ElectroCorticoGraphy (ECoG) that is used to control the spinal implant or Epidural Electric Stimulator (EES), to also power an Functional Electric Stimulation (FES) system and thereby further improve walking ability. Herein, it builds on earlier research which attempted the same without a Brain-Computer Interface (BCI). (Kobetic, R. et al., 1997)

**Research question / Hypothesis**

Does the addition of ECoG-controlled FES of the main muscles of locomotion (hip, knee and ankle flexors and extensors) to a BSI decreases time on the Time-Up and Go test (TUG test) after a single calibration session, in patients who have already undergone the complete ”Stimulation Movement Overground – Brain-Spine Interface” (STIMO-BSI) trial.

**Study design and approach**

**Study design**

Pilot study: single-site, single-arm, non-blinded, non-randomised, interventional, and will be executed at the University Hospital Lausanne (CHUV) in Switzerland

**Study population** (inclusion / exclusion criteria and approximate size of the group)

Inclusion: Participants equipped with the brain-spine interface system. Further in- and exclusion criteria of the clinical trials NCT04632290 and NCT06243952

Population size: 2 participants

**Variables** (most important ones including the primary outcome)

Primary outcome: time on TUG test

Secondary outcomes:

* Additional objective clinical gait assessment: 6-Minute Walk Test (6MWT), Berg Balance Scale (BBS) and Walking Index For Spinal Cord Injury II (WISCI II)
* Volitional muscle control as measured by maximal force production
* Subjective quality and ease of gait according to the patient as measured on a 10cm visual analogue scale

**Study methods** (description how the study will be carried out)

An algorithm for the conversion of ECoG data to FES of the correct muscles that correspond to the simultaneous spinal cord stimulation is created. Patients are included and informed consent is obtained. Patients are invited for an individual calibration session where a researcher (r1) applies the transdermal electrodes to the correct muscles and connects control thereof to the ECoG. Before turning on the FES, baseline measurements of all outcomes are performed by a researcher (r2). During the duration of the calibration session, various exercises are performed and the control of the FES is adjusted accordingly by a researcher (r1). After the session, baseline measurements are performed by the same researcher (r2), only the TUG is repeated 5 times with a randomised pattern of turning FES on and off (to which r1 is blinded). Between TUG repetitions, the participant is asked to walk a lap around the training hall to get reacquainted with the current FES settings. Data is collected, cleaned and analysed.

**Quantitative** (which statistical method) **or qualitative analyses** (which method)

A limited number of participants available for this analysis at the time of my internship will not provide sufficient statistical power to test the hypothesis. However, this experimental paradigm can be carried out in the upcoming participants of the study and a conclusion can be reached after the end of my stay. The statistical methods used here will thus form a preparation for the continuation of this experimental paradigm with a larger number of participants. In the same way that the experimental protocols and FES-BCI algorithms will be prepared in this pilot study and reused later, so too will the statistical algorithm be prepared and reused. Due to the invasive and expensive nature of the procedure, it is unlikely that a large number of participants will be recruited even after my stay. Furthermore, the choice of analysis serves to further my experience with these methods.

Statistical analyses:

* Descriptive statistics outlining the change in outcome values between baseline and post-session, as well as post-session with FES to post-session without FES for the TUG
* Bayesian mixed-effects model to account for intrasubject correlation. It takes both status and order (i.e., whether it was the first or fifth TUG repetition) as fixed effects, and using random intercepts to account for intrasubject correlation

Motivation: I do realise that using Bayesian statistics is not ordinary within medicine. However, I have taken a Bayesian statistics course for my Artificial Intelligence degree, and thus have some prior knowledge. With a normal (i.e., inter-subject) design, I would not be able to achieve any degree of statistical significance due to the population restrictions placed on the experiment due to the prerequisite of having participated in an earlier trial.

**Time Table**

Please mark applicable activities with an ‘X’) and, if necessary, expand the table with more relevant activities (and weeks).

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Week** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| Study of literature | X | X | X |  |  |  |  |  |  |  |  |  |
| Technical instruction / practise technique / learning specific lab skills | X | X | X |  |  |  |  |  |  |  |  |  |
| Preparation, logistics (A)\* |  | X | X | X | X |  |  |  |  |  |  |  |
| Taking measurements (B)\* |  |  |  | X | X | X | X | X |  |  |  |  |
| Data analyses / statistics  (C)\* |  |  |  |  |  |  |  | X | X | X |  |  |
| Write introduction |  |  | X | X | X |  |  |  |  |  |  |  |
| Write method |  |  |  |  |  | X | X | X |  |  |  |  |
| Write results |  |  |  |  |  |  |  |  |  | X | X |  |
| Write discussion |  |  |  |  |  |  |  |  |  | X | X |  |
| Prepare presentation |  |  |  |  |  |  |  |  |  |  | X | X |
| Oral presentation at host department |  |  |  |  |  |  |  |  |  |  |  | X |
| Preparation of algorithm : | X | X | X |  |  |  |  |  |  |  |  |  |
| … : |  |  |  |  |  |  |  |  |  |  |  |  |

\* A Please specify A (for instance: draw sample, invite/recruit subjects, etc.): Recruitment of subjects is done in week 2 and 3. Reservation of experimental space, recruitment of necessary researchers is done as soon as possible after recruitment

\* B Please specify B (for instance: extract data from records, conduct interviews, perform other measurements on study subjects, perform measurements on (bio)material, etc.): Perform sessions with subjects and perform measurements as specified above

\* C Please specify C: Between sessions with research subjects, perform preliminary descriptive and Bayesian analysis, so that the R code is prepared when the final data comes in. As soon as all data has been gathered, perform final analysis

**Feasibility**

Feasibility is highly dependent on domain specific knowledge. Due to my parallel degree in Artificial Intelligence, I have extensive programming experience and limited experience with BCI/signal processing. Furthermore, due to my ongoing completion of a 3-month elective clinical rotation in PMR, I have the prerequisite knowledge to start using the FES quickly.

The study however, is dependent on a number of factors:

* Availability of a second researcher and sufficient space to perform the sessions
* Availability of FES material
* Availability of and willingness to participate of people within the limited pool of possible participants

**Reference list of literature**

Lorach, H. et al. (2023) Walking naturally after spinal cord injury using a brain–spine interface. Nature, 618(7963), 126-133

De Rooij, I.J.M., et al. (2021) To What Extent is Walking Ability Associated with Participation in People after Stroke? J of Stroke, 30(11), 106081

Jeawon, M. et al. (2023) Exploring the Quality of Life of People with Incomplete Spinal Cord Injury Who Can Ambulate. Disabilities, 3(4), 455-476

Rodríguez-Fernández, A. et al. (2021) Systematic review on wearable lower-limb exoskeletons for gait training in neuromuscular impairments. J of NeuroEngineering and Rehab, 18(22)

Kobetic, R. et al. Muscle selection and walking performance of multichannel FES systems for ambulation in paraplegia. IEEE Trans Rehabil Eng, 5(1), 23-9