

Cover Page

Official Title: Safety and Efficacy of High-Channel Implanted
Brain-Computer Interface in Promoting Motor Function
Improvement in Patients with Tetraplegia

NCT Number: Not yet assigned

Document Date: 2025-09-20

Document Type: Informed Consent Form

Version: V3.0

Informed Consent Form

Participant Information Sheet

Study Title: Safety and Efficacy of High-Channel Implanted Brain-Computer Interface in Promoting Motor Function Improvement in Patients with Tetraplegia

Principal Investigator (This Center): Jing Ding

This Center: Zhongshan Hospital, Fudan University

Sponsor: Zhongshan Hospital, Fudan University

Dear Participant:

You are invited to participate in the study entitled Safety and Efficacy of High-Channel Implanted Brain-Computer Interface (BCI) in Promoting Motor Function Improvement in Patients with Tetraplegia. Please read this informed consent form carefully before deciding whether to participate. Participation is entirely voluntary, and you may only be enrolled after signing this informed consent form. If you have any questions about content you do not understand, you may ask your study doctor or research staff to explain it to you. We encourage you to discuss participation with your family and friends before making a decision. You have the right to refuse participation or to withdraw at any time without penalty or loss of entitled benefits. If you are participating in another study, please inform your study doctor or research staff. The background, purpose, study procedures and other important information are described below.

I. Study Background

Tetraplegia is a common manifestation of neurological disorders. Damage to the brainstem (BI, the hub connecting the brain and spinal cord, containing critical nuclei and tracts) or cervical spinal cord injury (SCI, the “main pathway” transmitting motor signals) can cause severe impairment of self-care ability and quality of life, increasing the burden on families and society. With rising incidences of trauma (traffic accidents, high-altitude falls) and cerebrovascular disease, cases of tetraplegia are increasing, making the study of its pathogenesis and rehabilitation strategies an important medical issue.

Brain-computer interface (BCI) technology establishes a direct communication channel between the brain and external devices. By recording neural activity such as electroencephalography (EEG) signals, algorithms decode user intentions and translate them into commands to control external devices, enabling actions consistent with voluntary intention (such as motor control or

communication). Currently, multiple clinical trials are exploring the safety and efficacy of BCI in people with SCI.

In this study, implanted intracranial electrodes are used as buried electrodes (unapproved device, National Medical Device Testing [Magnetism] No. QW2024-4421) designed to work with external EEG-signal receiving equipment to record and monitor deep-brain electrical activity. By surgically implanting “buried electrodes” into the cranium, deep cortical and subcortical electrophysiological activity (not accessible from the scalp surface) is captured and converted into storable, analyzable signal data, allowing real-time or dynamic observation of changes.

Our research team previously performed high-channel electrode implantation surgeries in two rhesus monkeys. Both short-term (12-day) and long-term (183-day) implantation showed no obvious scarring or angiogenesis on the brain surface, indicating no significant impact on safety in large animals. During implantation, the monkeys were able to use the BCI to control external devices such as a mouse for web browsing and gaming.

This study also uses epidural electrical stimulation (EES) with an implanted spinal cord stimulator and epidural electrode (approved devices, Registration Nos. 20203120516 and 20203120514) originally indicated for adjuvant treatment of refractory pain in the trunk and limbs. This study is an off-label use. Our team previously implanted spinal cord stimulation electrodes and stimulators in five SCI patients with paraplegia, preliminarily verifying safety for lower-limb motor dysfunction.

This project aims to use high-channel implanted intracranial BCI technology to decode motor intention with high precision and, through a pneumatic hand or EES, assist patients with BI or cervical SCI in restoring limb motor function and enhancing neuroplasticity. This is an exploratory trial with no therapeutic guarantee.

II. Study Objectives

Safety

To explore the safety of high-channel implanted BCI in rehabilitation of patients with tetraplegia.

Feasibility of Treatment Process

To explore the feasibility of the rehabilitation process using high-channel implanted BCI in patients with tetraplegia.

Tolerability

To explore the tolerability of high-channel implanted BCI in rehabilitation of patients with tetraplegia.

Efficacy

To explore the effectiveness of high-channel implanted BCI in improving motor function in patients with tetraplegia.

III. Study Procedures

1. Number of Participants

Approximately 10 participants will be enrolled at Zhongshan Hospital, Fudan University.

2. Study Steps

If you agree to participate, you will sign this informed consent form. The study is divided into three phases: a 3-month main study phase, a 3-month extension phase, and a 3-month follow-up phase. The main study phase includes screening/baseline, preoperative preparation, surgery (intracranial electrode implantation), upper-limb rehabilitation adjustment, and pneumatic hand function training. The extension phase includes upper-limb efficacy evaluation, epidural test electrode and stimulator implantation, and limb function training. The follow-up phase includes intracranial electrode removal, long-term epidural electrode implantation, and remote guidance. This clinical trial has no randomized control group; all participants receive the same experimental intervention.

2.1 Main Study Period

Screening/Baseline Phase

The screening period lasts approximately one week. After signing this informed consent form, you will undergo one week of noninvasive scalp EEG-based brain-controlled training once per day for about 1–2 hours each time. Demographic data, height, weight, medical history and previous laboratory results will be collected. Eligibility criteria will be confirmed and your physical condition comprehensively assessed with additional laboratory and imaging tests, especially motor function of the limbs (e.g., muscle strength, severity of BI or SCI) and neurological function.

Baseline assessments include:

- Manual muscle testing
- Modified Ashworth spasticity score
- 3-meter walking time
- Motion-capture gait analysis (step width, step length, step height, cadence, speed)
- Plantar pressure values
- Bilateral lower-limb muscle volume
- Visual analog scale (VAS) for pain

- Sexual Health Inventory for Men (SHIM)/Screening Tool for Female Sexual Dysfunction (SCS-W)
- International Consultation on Incontinence Questionnaire Short Form (ICIQ-SF) and International SCI Bowel Function Basic Data Set
- 128-channel EEG
- Electromyography (EMG)
- Somatosensory evoked potentials (SEP)
- Functional Magnetic Resonance Imaging (fMRI)

Preoperative Preparation Phase

Based on screening results, a preoperative discussion will be held. You will sign a surgical informed consent form and a surgical plan will be developed to determine electrode implantation sites.

Intracranial Electrode Surgery Phase

Under general anesthesia, intracranial electrodes will be implanted according to the preoperative plan. The entire procedure typically lasts about 3–4 hours and includes:

- Craniotomy: Incise the scalp at the predetermined site, dissect the periosteum, use a cranial drill and milling cutter to create and remove a bone flap, open the dura mater, and expose the brain tissue.
- Electrode Placement: Place the cortical electrodes directly on the brain surface as planned, ensuring accurate positioning.
- Closure and Fixation: Secure and externalize electrode leads, suture the dura, replace and fix the bone flap, and close the scalp in layers.
- Chest Pulse Generator Placement: In the subclavian area, disinfect and prepare the site; make a 3–4 cm incision to create a subcutaneous pocket, tunnel the extension leads from the intracranial electrodes to the chest, place the pulse generator into the pocket, and suture it after confirming signal integrity..

The implanted electrodes are buried electrodes (not yet marketed, National Medical Device Testing [Magnetic] No. QW2024-4421) used with an external EEG-signal receiver to record and monitor deep-brain electrical activity. They capture neurophysiological signals from subcortical areas (not accessible from the scalp surface), convert them into storable, analyzable data, and allow real-time or dynamic observation. Intraoperatively, electrode impedance will be tested to confirm integrity and connectivity, and neurophysiological monitoring performed to confirm position. Within two hours postoperatively, a head Computed Tomography (CT) scan will be performed to verify electrode position again. Within 24 hours postoperatively, electrocardiographic monitoring will be performed to observe vital signs, consciousness, and assess safety.

Upper-Limb Functional Training Phase

Beginning 24 hours after surgery, researchers will test electrode impedance daily to ensure integrity and connectivity. Beginning one week after surgery, you will undergo approximately 11 weeks of upper-limb training using a buried intracranial EEG-controlled continuous passive motion device. This involves attempted movement tasks to build a motor-intention decoding model; decoded signals will drive the device to perform hand joint movements—slow, continuous, brain-controlled passive flexion, extension or rotation—twice daily for about 1–2 hours per session. Session number and total time will be adjusted according to your condition. Basic rehabilitation includes neuromuscular electrical stimulation, pneumatic therapy, mat exercises, and sitting-balance training once daily for about 30 minutes. Throughout the period from electrode implantation to removal, researchers will closely monitor for complications such as infection, bleeding, or electrode displacement. Wound dressings will be changed every five days.

2.2 Extension Period

Upper-Limb Function Evaluation Phase

Evaluation includes:

- Grasping Success Rate: Percentage of successfully completed designated grasping tasks.
- Object Type Coverage: Ability to accurately grasp various objects such as cups, phones, and paper.
- BCI Command Recognition Accuracy: Correctness of translating EEG signals into grasping commands.
- Grasping Delay Time: Interval from brain grasping intention to action execution.
- Clinical Function Assessment: Manual muscle testing, Modified Ashworth spasticity score, 3-meter walking time, motion-capture gait data, plantar pressure testing, VAS, SHIM/SCS-W, ICIQ-SF for urinary retention, and bowel function scale.
- Ancillary Examinations: Limb muscle Magnetic Resonance Imaging (MRI), EEG, Electromyography (EMG), Somatosensory Evoked Potentials (SEP), and head Functional Magnetic Resonance Imaging (fMRI).

Evaluation frequency:

- Every 3 days: grasping success rate, object coverage, BCI command recognition accuracy, grasping delay time.
- Monthly: clinical function assessment.
- Every 3 months: ancillary examinations.

Stimulator Test Phase

After signing the surgical consent for the spinal cord test stimulator, surgery will generally be performed within one week depending on your condition and hospital schedule. Under general anesthesia, the test stimulator and epidural electrodes will be implanted. The procedure usually lasts 3–4 hours and includes:

- Incision: Make a small incision next to the target spinal segment or percutaneously puncture the epidural space (potential space between the dura mater and spinal cord); confirm correct location.

- **Electrode Placement:** Insert the electrode through the puncture channel or incision into the epidural space and adjust its position to cover the target spinal segment.
- **Fixation and Suturing:** Secure the electrode leads, connect the extension leads, tunnel subcutaneously to the external test stimulator, and suture the incision.

The epidural electrode and rechargeable spinal cord stimulator (Registration Nos. 20203120516 and 20203120514) are approved devices for adjuvant treatment of refractory pain in the trunk and limbs; this study uses them off-label. Intraoperatively, electrode impedance testing, X-ray monitoring, and neurophysiological monitoring will be performed to confirm position. Within two hours postoperatively, spinal CT will verify electrode placement again. Within 24 hours postoperatively, electrocardiographic monitoring will assess vital signs and consciousness. Throughout the period from implantation to removal, researchers will closely monitor for infection, bleeding, or electrode displacement. Wound dressings will be changed every other day.

Limb Function Rehabilitation Phase

Beginning 24 hours after spinal cord test stimulator implantation, researchers will test electrode impedance daily. Starting 24 hours post-implantation, you will undergo about 21 days of combined upper-limb training (as above) and spinal-stimulation-driven lower-limb training, building a motor-intention decoding model. Decoded signals will drive the upper-limb device and spinal stimulator to control limb movements. Upper-limb training focuses on slow, continuous, brain-controlled passive flexion, extension or rotation of the hand joints twice daily for one hour per session. Lower-limb training will be chosen according to your rehabilitation status, including supine leg lifts, standing leg lifts, and suspended stepping once daily for two hours per session. Session number and duration will be adjusted to your condition. Basic rehabilitation (neuromuscular electrical stimulation, pneumatic therapy, mat exercises, sitting training) continues once daily for 30 minutes. At the end of this buried-EEG-controlled limb function training, grasping success rate, object coverage, BCI command recognition accuracy, grasping delay time, clinical function assessments and ancillary examinations will be repeated.

2.3 Follow-Up Period

Intracranial Electrode Removal Phase

At 180 ± 3 days after intracranial electrode implantation, electrodes will be removed. If you do not opt for long-term spinal cord stimulator implantation, the intracranial electrode and spinal cord test stimulator with epidural electrode will be removed simultaneously. If you opt for long-term spinal cord stimulator implantation, the intracranial electrode will be removed while the epidural electrode is retained and the test stimulator replaced with a permanent spinal cord stimulator. The entire procedure usually lasts 2–3 hours and includes:

- **Intracranial Electrode Removal:** Under general anesthesia, disinfect the surgical site, locate the electrodes, make a small incision to expose them, gently remove along the original path, achieve hemostasis, suture, and dress the wound.
- **Epidural Electrode Removal:** Under general anesthesia, disinfect and drape, locate the electrode entry site, make a small incision, expose the external part of the electrode, gently

grasp and slowly remove it along the original path, achieve hemostasis, suture, and dress the wound.

- Conversion to Permanent Spinal Cord Stimulator: Under local anesthesia, disinfect, locate the electrode entry and external stimulator connection site, incise the skin, separate tissues, expose the electrode and temporary stimulator connection, disconnect, connect the electrode to the implanted permanent pulse stimulator, place the stimulator subcutaneously, confirm normal device function, achieve hemostasis, suture, and dress the wound.

Noninvasive Scalp EEG–Controlled Training Phase

If you undergo permanent spinal cord stimulator implantation, starting 24 hours post-surgery, researchers will test electrode impedance daily and begin approximately 14 days of scalp EEG-controlled training to drive spinal stimulation of limb movements. This involves movement-attempt tasks to build a motor-intention decoding model; decoded signals drive the spinal stimulator to activate limb movement. Training content will be selected according to your rehabilitation status, including supine leg lifts, standing leg lifts, and suspended stepping once daily for two hours per session. Session number and duration will be adjusted as needed. Basic rehabilitation (neuromuscular electrical stimulation, pneumatic therapy, mat exercises, sitting training) continues. At the end of scalp EEG-controlled training, grasping success rate, object coverage, BCI command recognition accuracy, grasping delay time, clinical function assessments and ancillary examinations will be repeated.

Remote Guidance Training Phase

If you receive a permanent spinal cord stimulator, about two weeks post-surgery you will be discharged and begin a 3-month remote-guided training program:

- Weeks 1–4: Adaptation to stimulation, scheduled turning, passive hip–knee–ankle movement.
- Weeks 5–8: Leg lifts, ankle exercises, core strengthening, and sitting-balance training.
- Weeks 9–12: Wheelchair transfers, standing, daily skill learning, spasticity management.

Progression will be individualized, including suspended lower-limb rehabilitation training. After the remote-guided follow-up period, grasping success rate, object coverage, BCI command recognition accuracy, grasping delay time, clinical function assessments and ancillary examinations will again be performed.

If you decide to participate, you will need approximately 6 months of hospitalization. During hospitalization, EEG, EMG, and functional test scales will be used to assess your cognitive and physical capacity to continue training. After discharge, you will return for follow-up once a month for a total of three visits.

3. Duration of the Study

The overall study is planned to last about 3 years. Your participation in this study will last approximately 9 months.

You may choose to withdraw from the study at any time without losing any benefits to which you are otherwise entitled. However, if you decide to withdraw during the study, we encourage you to discuss this with your physician first. If you experience a serious adverse event or your study doctor believes that continued participation is not in your best interest, he or she may decide to withdraw you from the study. The sponsor or regulatory authorities may also terminate the study during its course. Your withdrawal will not affect your normal medical care or rights.

If you withdraw from the study for any reason, and if deemed necessary by your doctor, you may be asked to undergo a final laboratory test and physical examination to ensure your safety.

4. Collection of Biological Samples

This study will not collect any additional biological specimens.

IV. Risks and Benefits

1. What Are the Risks?

Participation may involve the following risks. You should discuss these risks with your study doctor or, if you wish, with your regular healthcare provider.

Known Risks

Risks of Intracranial Electrode Implantation and Removal:

- **Bleeding and Hematoma:** Surgical injury to cerebral blood vessels may cause intracranial hemorrhage or hematoma formation, which can compress surrounding brain tissue and result in neurological deficits such as limb weakness, speech impairment, or altered consciousness, and in severe cases may be life-threatening.
- **Infection:** All invasive procedures carry a risk of infection at the incision, within the cranium, or at the electrode site. Intracranial infection is a serious complication and may cause meningitis, brain abscess, fever, headache, vomiting, seizures, or further brain damage, and can be life-threatening.
- **Nerve Injury:** During electrode implantation or removal, surrounding neural tissue may be directly damaged, leading to sensory abnormalities, motor deficits, or impairment of vision or hearing, depending on the site of injury.
- **Seizures:** Surgical manipulation and the presence of electrodes may provoke seizures, which vary in frequency and severity and may affect quality of life and rehabilitation progress.
- **Electrode Migration or Malfunction:** Electrodes may shift postoperatively, reducing accuracy of stimulation or recording, or may fail (e.g., breakage, short-circuit), necessitating revision surgery.

Risks of Epidural Electrode Implantation and Removal:

- **Bleeding:** Injury to epidural vessels may lead to epidural hematoma, which, if not promptly managed, can compress the spinal cord or nerve roots and cause sensory or motor deficits such as numbness, weakness, or bladder/bowel incontinence.
- **Infection:** Similar to deep brain electrodes, epidural electrode procedures carry infection risk, which may extend to the epidural space and cause epidural abscess, potentially resulting in myelitis and impaired neurological function if untreated.
- **Spinal Cord or Nerve Injury:** Accidental damage to the spinal cord, nerve roots, or peripheral nerves during placement or removal may result in pain, numbness, or weakness in the affected area.
- **Cerebrospinal Fluid (CSF) Leak:** Dural injury may cause CSF leakage, leading to low-pressure headaches, dizziness, nausea, vomiting, and increased infection risk.
- **Electrode-Related Issues:** Electrodes may migrate, extrude, or malfunction, leading to inaccurate stimulation or requiring reimplantation or replacement.
- **Implant Site Problems:** Long-term subcutaneous pulse generators may cause local pain, swelling, migration, or skin breakdown due to placement or tissue reaction.
- **Pain and Discomfort:** Postoperative pain or discomfort at the electrode site may occur from surgical trauma or electrode irritation and may impact rehabilitation and quality of life.

Potential Risks

Brain–Spine Interface (BSI) Decoding Risks:

- **Signal Interference:** BSI devices depend on precise neural signal acquisition and decoding. Biological signals are weak and easily affected by external electromagnetic interference (phones, computers) and internal circuit noise, impairing decoding accuracy.
- **Device Failure:** BSI devices are complex electronic systems prone to hardware faults (electrode breakage, short circuits) or software errors (algorithm faults, crashes), which may disrupt function or cause accidental harm (e.g., battery depletion causing sudden device stop).
- **Decoding Errors:** Current decoding technology is still evolving. Complex neural patterns may not be fully decoded, causing incorrect responses (e.g., imprecise prosthetic movement, erroneous BCI interaction).
- **Privacy Risks:** Excessive brain-signal capture may risk exposure of subconscious thoughts or emotional tendencies.

Rehabilitation Risks:

- **Physical Injury:** Improper training may cause musculoskeletal injury or exacerbate neurological damage; weak or cardiac patients may have cardiovascular risk.
- **Infection:** Poor wound care increases infection risk; immobility may predispose to respiratory infection.
- **Psychological Issues:** Difficulty of rehabilitation may cause anxiety, depression, or frustration if expectations are unmet.
- **Other Risks:** Falls or accidents during training.

2. What Are the Benefits?

Decoding your motor intentions with external device assistance may potentially restore or substitute some neural functions, but benefits cannot be guaranteed.

- Upper-Limb Motor Function: Capturing brain motor commands and using passive motion devices or electrical stimulation may enable voluntary grasping.
- Lower-Limb Motor Function: Targeted stimulation may prevent atrophy, increase strength and endurance, and improve self-care; decoding motor commands may also enable assisted standing or walking.
- Potential Additional Benefits: Sensory improvements (position, touch, pain perception); autonomic improvements (bladder, bowel control); psychological and social benefits (increased independence, confidence, reduced burden). These are not guaranteed because the trial is exploratory.

However, because this is an exploratory study, none of the above benefits can be fully guaranteed.

V. Alternative Treatment Options

Instead of participating, you may receive conventional therapy provided by your physician, such as neuromuscular electrical stimulation training, lower-limb pneumatic therapy, mat exercises, and sitting-balance training.

VI. Confidentiality of Personal Information

During the study, the research team may need to access your medical history, past records, and test results. By signing this consent form, you authorize the team to obtain necessary medical information from your other providers. Only authorized study staff can access your identifiable information. Ethics committees and regulators may review original medical records to verify trial data.

Your personal information and study data will be coded to remove direct identifiers (name, contact details). Published papers or conference reports will not disclose identifiable information.

You may withdraw permission for use and sharing of your personal information at any time by contacting your study doctor. After withdrawal, no new identifiable data will be collected, but existing coded data may still be used and shared with research partners (including Lingang Laboratory) as described in this form. For scientific validity, you may not be able to access certain study records until the study ends. After the study, you may request your health data and correct any errors. Data will be stored coded at Zhongshan Hospital for five years before destruction.

Coded data will be transmitted to Lingang Laboratory for analysis of motor intention from neural activity, supporting BCI research.

VII. Feedback of Study Results

You will be provided your laboratory test results (blood and urine routine, stool with occult blood, blood biochemistry, coagulation, ECG, etc.).

The overall study results (without personal information) will be posted on ClinicalTrials.gov after completion; you may search by study title keywords.

VIII. Study Costs and Related Compensation

1. Costs of Study Drugs/Devices and Related Examinations

Hospitalization fees, surgery fees, all trial-related drugs, rehabilitation devices, laboratory tests, and nursing care during the trial are provided free of charge. Treatment and tests for other conditions are not covered. Medical devices used (high-channel buried electrodes, passive motion device, spinal cord test stimulator, epidural electrode, permanent epidural stimulator with 9-year life) are free. After remote-guided training, the hospital will provide long-term EEG monitoring, EMG tests, neurological evaluations, and ancillary tests free of charge.

2. Compensation for Injuries

No extra compensation is provided for participation. However, if study-related injury occurs, free treatment will be provided by the sponsor and compensation under Chinese law. The study has purchased clinical trial liability insurance from Ping An Property Insurance Co. of China; compensation for study-related injury will be paid by insurance, with uncovered parts borne by the sponsor.

IX. Participants' Rights and Related Precautions

1. Your Rights

Participation is voluntary. Declining will not affect your other treatments. You may withdraw at any time without discrimination or unfair treatment. If new information arises affecting your rights or safety, you will be asked to sign an updated consent form.

2. Notes

You will be asked to provide truthful medical history and current health information; report any discomfort during the study; avoid restricted drugs/foods as instructed; inform your doctor of participation in any other studies.

X. Contact Information for Inquiries

If important new information arises that may affect your willingness to continue, your doctor will promptly inform you. For questions about your data or to learn study results after completion, you may contact Dr. Chen at TEL: +86 18317089097.

This study has been approved by the Ethics Committee. For any issues about your rights or to report difficulties, dissatisfaction, or provide suggestions, contact the Ethics Committee of Zhongshan Hospital, Fudan University at 021-31587871 or email ec@zs-hospital.sh.cn.

Participant Signature Page

Informed Consent Statement:

I have been informed of the study's purpose, background, procedures, risks, and potential benefits. I have had enough time and opportunity to ask questions and am satisfied with the answers. I agree to participate in this study.

I have been told whom to contact if I have questions, concerns, or suggestions, or wish to assist with the study.

I understand that I can choose not to participate or withdraw at any time without giving a reason.

I understand that if my condition worsens, I experience serious adverse events, or my doctor deems continued participation not in my best interest, he/she may withdraw me from the study. The sponsor or regulatory agencies may also terminate the study without my consent. If this happens, my study doctor will promptly notify me and discuss my options.

I will receive a copy of this Informed Consent Form containing the signatures of both myself and the investigator.

I understand that participation requires use of my personal information. I agree to the use and processing of my personal information as described in this consent form.

☐ Agree

☐ Disagree, and unable to participate in this study.

Participant's Signature: _____

Date: _____

Legal Guardian's Signature: _____

Date: _____

Relationship to Participant: _____

(Required if the participant lacks or has limited capacity for informed consent; signature and date of the guardian are needed.)

Impartial Witness's Signature: _____

Date: _____

(Required if the participant cannot read this Informed Consent Form; an impartial witness must attest that the investigator has explained all contents of the form to the participant and that the participant has expressed willingness to participate.)

Investigator's Signature: _____

Date: _____