Single-Center Randomized Controlled Clinical Trial of Intradermal Acupuncture for Ocular Surface Disease Secondary to Intractable Peripheral Facial Paralysis

Lead Research Site: Zhejiang Provincial Hospital of Traditional Chinese Medicine

Principal Investigator (PI):

In accordance with the *Measures for the Administration of Clinical Research Projects Conducted by Medical and Health Institutions* (2014 Edition), the Principal Investigator shall be the person in charge of the relevant professional department or a health professional with an associate senior professional title or above. Generally, there is only one Principal Investigator for each project, and the rest are co-investigators.

Statistical Analysis Unit:

Protocol Version Number: 3.0

Protocol Version Date: March 15, 2026

Confidentiality Statement

CATALOGUE

Visit Schedule

	Screening Period	Intervention Period (4 weeks)			Follow-up Period(6 weeks)		
		Enrollment	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Visit Phase	V_0	V_1	V_2	V_3	V_4	V_5	V_6
Visit Time	week-1	week0	week2	week4	week6	week8	week10
Informed Consent Form	Δ						
Demographic Information [A]	Δ						
Medical History [B]	Δ						
FNGS 2.0 [C]	Δ		Δ	Δ	Δ	Δ	Δ
ENoG [D]	Δ						
OSDI[E]	Δ		Δ	Δ	Δ	Δ	Δ
Ocular Surface Function Test [F]	Δ			Δ			Δ
The Width of Palpebral Fissure Incompleteness [G]	Δ		Δ	Δ	Δ	Δ	Δ
Adverse Events	Δ	Δ	Δ	Δ	Δ	Δ	Δ
Blinded Assessment		Δ		Δ			

Notes:

A. Demographic statistics include the patient's date of birth, gender, ethnicity, and other relevant information.

B. Medical history includes past and present medical histories of facial paralysis and ocular diseases secondary to facial paralysis.

C. Facial Nerve Grading System 2.0[1]: A standardized tool for quantitatively assessing the severity of facial nerve dysfunction, optimized from the House-Brackmann (H-B) Facial Nerve Grading Scale. It achieves objective evaluation of facial nerve function through precise itemized

scoring and is a commonly used quantitative scoring system for facial nerve function in clinical practice and scientific research.

D. Electroneuronography (ENoG)[2]: The maximum compound muscle action potential (CMAP) amplitudes of the facial nerve on the healthy and affected sides are detected via electroneuronography, and the ratio of the amplitude on the affected side to that on the healthy side is calculated. Essentially, the healthy side serves as an internal normal control to reflect the severity of nerve injury on the affected side. A lower ratio indicates fewer nerve fibers with effective signal conduction on the affected side and more severe nerve injury.

E. Ocular Surface Disease Index (OSDI)[3]: The OSDI questionnaire is a self-assessment questionnaire for quantitatively evaluating the impact of OSD on patients' quality of life.

F. Ocular Surface Function Test: Includes tear meniscus height, tear break-up time (TBUT), and meibomian gland analysis.

G. Width of palpebral fissure incompleteness refers to the horizontal fissure distance between the upper and lower eyelid margins that fails to fully adhere when the eyelids are closed naturally or with maximum force. It is a core quantitative indicator for evaluating eyelid closure function, with the unit usually being millimeters (mm).

1. Research Background

Intractable facial paralysis(IFP) generally refers to PFP(PFP) that does not show significant recovery after conventional treatment, clinically manifesting as unilateral deviation of the mouth and eye, incomplete eyelid closure, unilateral facial muscle synkinesia, malposition, etc. This condition is mostly caused by severe facial nerve injury in PFP, or delayed, prolonged, or incorrect initial treatment[4]. PFP is a common clinical disease caused by inflammation, acute edema, and compression of the facial nerve within the stylomastoid foramen due to cold exposure, viral infection, and other factors. Bell's Palsy (BP) is the most representative type, accounting for approximately 95% of clinical PFP cases. One in 60 people will develop BP at some stage of life, with an annual incidence of 11.5–53.3 cases per 100,000 people[5]. Studies have shown that approximately 60%–87% of patients with IFP fail to achieve

full recovery[6], developing sequelae or permanent paralysis. However, the definition of IFP has not been clearly unified. Electroneuronography (ENoG) is a widely recognized important reference indicator for the prognosis of PFP[7], which records CMAP of facial muscles after electrical stimulation of the main facial nerve trunk via surface electrodes. Studies indicate that patients with an affected/healthy CMAP amplitude ratio <20% generally have a recovery period of no less than 4 months, and most experience incomplete recovery[8]. Therefore, this study mainly enrolls PFP patients with a CMAP amplitude ratio <20%.

Due to severe facial nerve injury and a long recovery cycle, IFP is often accompanied by a variety of associated OSD(OSD), among which incomplete eyelid closure, epiphora, and ocular motor dysfunction are the most common. These can lead to exposure keratitis, conjunctivitis, and even vision loss[9][10], severely affecting patients' daily work. In modern life, electronic products have become a necessity for work, study, and social interaction, and patients cannot avoid using them, which further exacerbates ocular injury[11]. Meanwhile, high-frequency use of electronic products leaves no time for the damaged corneal epithelium to repair, and the superimposed effects of electronic products transform ocular surface injury from intermittent to persistent. Currently, there are no clearly recommended therapeutic drugs for PFP PFP in recovery guidelines, and Sodium Hyaluronate Eye Drops and other symptomatic supportive treatments are commonly recommended for associated OSD[9][12]. However, long-term corneal exposure combined with electronic product use in these patients renders the clinical efficacy of artificial tears unsatisfactory. Therefore, exploring an "effective, safe, convenient, and sustained" treatment method has important clinical value and can solve the long-term ocular problems accompanying IFP in these patients.

Acupuncture is a treasure of traditional Chinese medicine (TCM). Studies have shown that electroacupuncture and other therapies can effectively improve clinical symptoms in patients with dry eye syndrome[13]. But they have limitations such as high requirements for operator skills, poor patient treatment adherence, and short-lasting effects. As an important component of acupuncture therapy, intradermal

acupuncture(IA) achieve the regulation of meridian qi and blood and improvement of visceral function through subtle, sustained acupoint stimulation, featuring good efficacy, simple operation, minimal trauma, and high safety[14]. A literature review reveals a lack of high-quality clinical studies on IAtherapy for OSD after IFP. Preliminary pilot experiments by the research team indicate that IA can effectively improve OSDI scores in patients with OSD after IFP. To further verify the efficacy and safety of this treatment method, we will conduct a single-center, randomized, single-blind, placebo-controlled parallel trial, aiming to provide a convenient, safe, and easily promotable treatment for OSD after IFP. This treatment is simple and feasible, suitable for application in primary medical institutions and home-based rehabilitation of patients, helping to reduce the medical burden on medical institutions and patients, with important practical application value and promotion prospects.

2. Research Objectives

(1) Primary Objective

To preliminarily evaluate the effective rate of IA intervention for OSD after IFP through a single-center, randomized, single-blind, placebo-controlled parallel trial, and to provide a new effective treatment for ocular diseases secondary to intractable PFP.

(2) Secondary Objectives

To assess whether IA intervention exerts a synergistic promoting effect on improving patients' ocular symptoms, restoring ocular surface function, and facilitating facial nerve function recovery; to clarify the operational feasibility, safety, and patient acceptance of IA intervention, and to provide an optimized clinical treatment protocol.

3. Research Hypothesis

IA intervention can effectively improve the clinical symptoms of OSD after IFP, promote the recovery of ocular surface function (ocular indicators such as tear meniscus height and tear break-up time), and accelerate the recovery of ocular motor function. Compared with conventional treatment methods, IA intervention can more safely, effectively, and conveniently improve the clinical effective rate of treating OSD after IFP.

4. Study Design

This study adopts a single-center, randomized, single-blind, placebo-controlled parallel design, conducted at Zhejiang Provincial Hospital of Traditional Chinese Medicine. Conventional acupuncture therapy in the recovery phase and supportive treatment for OSD serve as the basic treatment regimen, with the innovative introduction of IA intervention for OSD after IFP. Block randomization is performed using the hospital's central randomization system, with dynamic balanced randomization of enrolled patients stratified by age and disease course. Patients are randomly assigned to the IA group and the sham intradermal acupuncture(SIA) group at a 1:1 allocation ratio. The total expected duration of participation for each subject is 10 weeks (4 weeks of intervention and 6 weeks of follow-up period). During the treatment phase, both groups receive consistent basic treatment; the IA group receives regular IA compression stimulation, while the SIA group receives SIA treatment. The SIA are produced by the same company as the IA needle with identical appearance, but the needle body is replaced with a thin silicone pad. Acupoint selection and operation are identical to those of the IA group. A WeChat mini-program named "Facial Paralysis Ocular Comfort Smart Assistant" is used during treatment to assist patients in performing independent IA compression. Single-blinding is implemented throughout the study: subjects, outcome assessors, and statisticians are unaware of group allocation. The preliminary efficacy and safety of IA intervention are verified through a scientifically designed trial.

Study interventions are performed by operators with more than 5 years of medical experience; the specific intervention protocol is detailed in the Study Intervention section below.

5. Randomization and Blinding

(1) Randomization

This study adopts block randomization using the hospital's central randomization system, with dynamic balanced randomization of enrolled patients stratified by age and disease course. Patients are randomly assigned to the IA group and the SIA group at a 1:1 allocation ratio. The randomization protocol is generated by the hospital's Clinical Evaluation Center. When a subject meets the inclusion/exclusion criteria and enters the study, the researcher performs randomization; this researcher is not involved in the statistical analysis of this project. The randomization protocol and all parameters set during its generation are collectively referred to as the blinding list, which is sealed and signed by the randomization protocol generator and kept by a dedicated staff member of the Clinical Evaluation Center who is not involved in this project. The central randomization system has strict access permissions; no one except the highest-level system administrator has the right to view the randomization protocol in the system.

(2) Blinding

In line with the principle of blinding, single-blinding is adopted due to the involvement of acupuncture operations. The clinical research coordinator is aware of patients' group allocation and provides limited information to each researcher. Researchers conducting assessments are unaware of group allocation and only ask simple questions critical for completing case report forms. Each subject receives treatment at different times to prevent information exchange. Treaters minimize conversation with subjects. Data statisticians are unaware of allocation information and independently complete statistical analysis, ensuring independent work of all researchers.

6. Sample Size

This study aims to demonstrate that the efficacy of the IA group is superior to that of the SIA group. Sample size calculation is based on the principle of superiority testing and completed using PASS 2025 software (Version v2025). Based on the research team's preliminary pilot results, the expected effective rate (P2) of the SIA group is set at 30% (0.3), and the expected effective rate (P1) of the IA group is set at 75% (0.45).

A clinically recognized superiority margin of 0.1 is set; the significance level (α) for the two-sided test is 0.0125 (adjusted from the original α=0.05 to control Type I error in multiple comparisons), and the test power is 80%. The calculated required sample size per group is 31 cases, with test power >0.8.

This study design includes two groups: the IA group and the SIA group. In addition, a dropout rate of approximately 20% is considered based on the total sample size. With a 1:1 group allocation, at least 39 patients are recruited per group, with a total of at least 78 patients to be recruited.

7. Subject Recruitment

This study has been approved by the Ethics Committee of Zhejiang Provincial Hospital of Traditional Chinese Medicine. All patients are recruited from the outpatient and inpatient departments of Zhejiang Provincial Hospital of Traditional Chinese Medicine from March 2026 to March 2027, with a total of 78 patients meeting the inclusion and exclusion criteria. Patients are randomly divided into two groups: the IA group and the SIA treatment, with 39 patients in each group.

8. Study Subjects

(1) Diagnostic Criteria

Diagnostic criteria for PFP[15]: Main manifestations include paralysis of facial expression muscles, disappearance of forehead wrinkles on the affected side, paralysis of the orbicularis oculi muscle, inability to close or incomplete closure of the

palpebral fissure, shallow nasolabial fold, drooping mouth angle, deviation of the mouth angle to the healthy side when showing teeth, and food retention between the teeth and cheek on the affected side during mastication.

(2) Inclusion Criteria

① Aged 18–65 years, regardless of gender; ② Meets the diagnostic criteria for PFP[15], disease course ≥1 month and ≤1 year, FNGS 2.0 score ≥15 points[6][7], and ENoG-derived maximum CMAP amplitude ratio of the zygomatic branch (ocular branch) of the facial nerve between the affected and healthy sides ≤20%[8][16]; ③ Has at least one subjective ocular symptom (dryness, foreign body sensation, burning sensation, fatigue, discomfort, red eye, fluctuating vision) and an OSDI score of 30–80 points[17]; ④ Voluntarily signs the informed consent form and can cooperate with the completion of treatment and follow-up.

(3) Exclusion Criteria

Patients meeting any of the following criteria will be excluded: ① Complicated with other underlying ocular diseases (glaucoma, keratitis, retinopathy, etc.), or acute inflammation or pathological conditions of the conjunctiva, sclera, eyelid, or cornea; ② Underwent intraocular surgery or laser therapy within 90 days; ③ History of systemic or topical antibiotic use or use of drugs affecting tear secretion within 3 weeks; history of dry eye medication use within 2 weeks; ④ Patients with lacrimal duct obstruction, lacrimal sac/nasolacrimal duct stenosis (positive Jones test), closed lacrimal puncta, or inability to fully close the eye due to damage to the nerve reflex arc; ⑤ Coagulopathy (thrombocytopenia, coagulation factor deficiency, etc.) or skin damage/infection at the intervention site; ⑥ Allergy to IA materials (stainless steel, medical adhesive tape); ⑦ Pregnant or lactating women; ⑧ Complicated with severe cardiac, hepatic, renal diseases, mental illness, or malignant tumors; ⑨ Participated in other clinical studies within the past month.

9. Study Intervention

(1) Interventional Treatment

① IA Group

Acupoint Selection: bilateral GB14, BL2, GB1, 6 acupoints in total

Acupuncture Operation: After the patient completes conventional acupuncture treatment for facial paralysis, the patient is instructed to sit or lie supine. The ocular acupoint skin is disinfected with 75% alcohol, and intradermal acupuncture (φ0.20*0.12mm, Seirin Press Needle, SEIRIN Corporation, Japan) are vertically inserted and embedded into the skin, avoiding blood vessels.

Treatment Frequency and Course: Needles are retained for 72 hours after insertion, followed by a 1-day rest. Needles are replaced after weekly acupuncture treatment for 4 consecutive weeks (8 sessions in total), with 4 weeks of follow-up after treatment completion.

Patient Operation Requirements: Patients log into the WeChat mini-program "Facial Paralysis Ocular Comfort Smart Assistant" to learn the standardized IA compression operation tutorial. The mini-program regularly reminds patients to perform IA therapy 3 times daily using a facial paralysis acupoint compression device, with an interval of approximately 4 hours between sessions. Patients can set their daily compression time independently; the mini-program sends timed reminders and indicates compression frequency. Each compression session lasts 3 minutes at a frequency of 60 compressions per minute. Compression intensity is adjusted to the patient's tolerance.

② SIA group

The SIA group receives intervention with SIA treatment. SIA and IA needles are both produced by SEIRIN Corporation (Japan) with identical appearance, but the needle body is replaced with a thin silicone pad. Acupoint selection, operation, and all other procedures are identical to those of the IA group.

Patient Operation Requirements: The same mini-program as the IA group is used, with identical treatment frequency, compression time, compression frequency, and compression intensity.

All treatment operations and informed procedures are performed in separate rooms for each patient to prevent communication and information exchange between patients.

(2) Basic Treatment

Both groups receive conventional treatment for PFP as usual, including conventional acupuncture therapy for PFP in the recovery phase and supportive treatment for OSD, as detailed below:

① Conventional Acupuncture Therapy for PFP in the Recovery Phase (based on previous clinical research results)

Acupoint Selection: Affected-side BL2, GB1, GB14, ST2, SI18, ST4, ST6, ST7, TE17, EN-HN16, EX-HN5, bilateral LI4.

Acupuncture Operation: Before operation, the patient is placed in a comfortable position accessible to the operator. The doctor thoroughly disinfects hands with hand sanitizer, then disinfects acupoint skin with 75% ethanol cotton balls from the acupoint center outward, ensuring a disinfection diameter of 2–3 cm. Acupuncture is performed after ethanol volatilization completely. Disposable acupuncture needles (specification: 0.25×40mm, Wujiang Jiachen Acupuncture Appliance Co., Ltd., Jiangsu Province) are used for routine acupuncture at all acupoints, with insertion depth adjusted to achieve local Deqi (needle sensation).

Electroacupuncture Operation: After routine acupuncture, a dedicated operator connects electroacupuncture devices to BL2-GB1 and ST6-ST4, applies discontinuous waves at 40Hz, and adjusts intensity to the patient's tolerance, with a timer set for 30 minutes.

Treatment Frequency and Course: Twice weekly, 30 minutes per session, for 10 consecutive weeks.

② Supportive Treatment Protocol for OSD

Sodium Hyaluronate Eye Drops (specification: 5mL:5mg (0.1%), Santen Pharmaceutical Co., Ltd., China) are administered to both eyes. Ocular contamination must be avoided during medication, and the drug must be used strictly in accordance with medical advice.

Treatment Frequency and Course: 3 times daily, 1 drop per time, for 10 consecutive weeks.

10. Study Flow

(1) Screening Phase

During the screening visit, the following procedures are performed:

Informed Consent: The study is explained in detail to the subject, and questions are answered before obtaining the patient's written and signed informed consent form. Laboratory tests and imaging assessments performed for routine clinical care prior to signing informed consent may be used if the data are within the specified window period. (If the study involves emergency situations where the subject or legal guardian cannot sign informed consent before the trial, this shall be clearly stated here.) All subsequent procedures are performed only after informed consent is obtained.

Demographic Statistics: Gender, date of birth, ethnicity, height, weight, body mass index (BMI);

Relevant Medical History: ① History of PFP with disease course ≥1 month and ≤1 year; ② History of OSD after IFP.

Auxiliary Examinations: ① Ocular Surface Disease Index (OSDI) score 30–80 points; ② Facial Nerve Grading System 2.0 score ≥15 points; ③ ENoG-derived maximum CMAP amplitude ratio of the zygomatic branch (ocular branch) of the facial nerve between the affected and healthy sides ≤20%.

(2) Randomization Phase

This study adopts block randomization using the hospital's central randomization system, with dynamic balanced randomization of enrolled patients stratified by age and disease course. Patients are randomly assigned to the IA group and the SIA group at a 1:1 allocation ratio.

(3) Treatment and Follow-up Phase

The treatment phase includes V_1 , V_2 , and V_3 , totaling 4 weeks. The following procedures are performed and indicators are collected during each treatment visit:

V_2 and V_3 : OSDI, FNGS 2.0, and width of palpebral fissure incompleteness are assessed.

V_3 : Additional ocular surface function examination, including TBUT and meibomian gland analysis.

(4) Observation Follow-up Phase

The 6-week period after the last treatment for all subjects constitutes the follow-up phase, with follow-up conducted every 2 weeks.

During each follow-up visit (V_4 , V_5 , V_6): OSDI, FNGS 2.0, and width of palpebral fissure incompleteness are assessed.

V_6 : Additional ocular surface function test, including TBUT and meibomian gland analysis.

Adverse event assessments are conducted at all study visit phases.

11. Subject Withdrawal or Study Treatment Termination

(1) Subject Withdrawal Criteria

Subjects will be excluded under the following circumstances: ① Dropout: Failure to complete observation for any reason. ② Non-compliance: Failure to receive embedding therapy as planned or non-adherence to medical advice. ③ Concomitant Intervention: Receipt of other treatments outside the study design during the treatment period. ④ Accident: Occurrence of severe IA embedding-related accidents.

If a subject withdraws midway, the reason for withdrawal shall be identified and recorded. The data will still be included in statistical analysis.

(2) Study Treatment Termination Criteria

The study will be terminated if major issues prevent its continuation, such as severe safety problems or severe funding shortages.

(3) Procedures for Subject Withdrawal or Study Treatment Termination

Efficacy and safety examinations shall be performed on the subject in accordance with the protocol provisions for withdrawal and final observation follow-up, and all adverse events (AEs) and outcomes shall be fully recorded. The researcher may recommend or provide alternative treatment methods to the subject based on their actual condition.

If the subject refuses further visit to the study center, follow-up of their survival status shall continue unless the subject revokes informed consent. In such cases, no further study assessments shall be conducted, and no additional data shall be collected.

12. Outcome Measures

(1) Primary Outcome Measure

Proportion of patients with a ≥12-point reduction in OSDI score from baseline after 4 weeks of treatment.

Note: According to previous related studies[17][18], the "Minimal Clinically Important Difference (MCID)" of the OSDI score is 10 points, with an MCID of 7.3–13.4 points for severe dry eye populations. Based on the study's pilot results, a 12-point reduction corresponds to "perceptibly significant improvement" in this study. Therefore, a ≥12-point reduction in OSDI score from baseline after 4 weeks of treatment is defined as "treatment response".

(2) Secondary Outcome Measures

① Ocular surface function test: TMH, TBUT and meibomian gland analysis; ② Width of palpebral fissure incompleteness; ③ Facial nerve function score: FNGS 2.0

(3) Other Evaluation Indicators

Adverse reactions related to acupuncture (bleeding, hematoma, needle syncope, pain at needle insertion site, infection, etc.) and adverse events caused by topical eye drops (eyelid pruritus, ocular irritation, conjunctival hyperemia, etc.) are recorded at any time.

13. Emergency Management

All acupuncture operations during the trial shall be performed under the guidance of a specialist or by a senior physician. If a patient experiences disease changes severely affecting daily work and life during treatment, an emergency adjusted treatment plan may be adopted after evaluation and diagnosis by a specialist, who will also assess whether to discontinue the study. Based on the characteristics of

PFP, an independent assessor unaware of group allocation evaluates the eligibility for electroacupuncture in the basic acupuncture protocol of this study before each acupuncture session using the Facial Nerve Grading System 2.0. If the grade is Grade I (4 points, complete recovery), or if facial muscle spasm, synkinesia, or malposition occurs, the assessor informs relevant staff to discontinue electroacupuncture in the corresponding area. No drugs are recommended in guidelines for PFP in the recovery phase, so no emergency medication is established. The date, time, and dosage of any treatments outside the study's prescribed protocol during the study period must be recorded promptly.

14. Study Supply Management

(1) Supply Receipt and Storage

Study supplies are uniformly procured by the sponsor, who shall provide complete qualification documents including quality certificates, production batch numbers, expiration dates, and instructions. After verification by researchers, supplies are warehoused and registered. A dedicated storage area is established with classified storage: intradermal acupuncture are placed in sealed, dry, light-proof special storage boxes to avoid extrusion deformation or contamination; Sodium Hyaluronate Eye Drops are refrigerated at 2–8°C, strictly prohibited from freezing and direct sunlight. Dual electronic and paper ledgers are established for all supplies, with detailed records of name, specification, quantity, batch number, expiration date, inbound/outbound time, recipient, and corresponding subject number to ensure full traceability.

(2) Supply Distribution and Retrieval

Supply collection follows the principle of "on-demand application and dedicated responsibility". Researchers collect corresponding supplies based on subject enrollment progress and treatment cycles with medical orders, verifying supply integrity and expiration date before collection, and signing confirmation after confirming no damage or deterioration. As an invasive intervention device, intradermal acupuncture must be used in an aseptic operating environment; unused

intradermal acupuncture are disposed of in accordance with medical waste regulations. As a prescription drug, Sodium Hyaluronate Eye Drops are distributed strictly in accordance with each subject's individualized treatment plan, with clear instructions on administration frequency, dosage, and precautions, and records of distribution time and subject signature.

(3) Drug Disposal Requirements

Regular supply inventory is conducted weekly to reconcile ledgers with actual inventory and ensure account consistency. Near-expiry supplies are specially marked and prioritized for use. Expired, damaged, or unqualified supplies are stored separately and uniformly disposed of in accordance with medical waste management regulations, with complete disposal records. The study strictly complies with GCP guidelines and hospital supply management requirements to prevent abuse, waste, or loss of supplies, ensuring the safety, efficacy, and traceability of clinical trial supplies and providing foundational support for the scientific validity of study results.

15. Adverse Events (AEs), Serious Adverse Events (SAEs), and Adverse Reactions (ARs)

(1) Definitions

Adverse Event (AE): Any untoward medical occurrence in a subject administered a test product, which may present as symptoms, signs, diseases, or laboratory abnormalities, but is not necessarily causally related to the test intervention.

Serious Adverse Event (SAE): Any untoward medical occurrence in a subject administered a test product that results in death, life-threatening risk, permanent or severe disability/functional loss, hospitalization or prolongation of hospitalization, congenital anomaly, or birth defect.

Adverse Reaction (AR): Any harmful or unintended reaction occurring in a clinical trial that may be related to the test intervention.

(2) Recording of AEs/SAEs

All AEs and SAEs occurring during the trial, regardless of causal relationship with the test intervention, shall be recorded in the original case records and case report forms (CRFs).

AE/SAE records shall include: event name, duration, severity, causal relationship judgment between the event and the test product, measures taken, and event outcome. The researcher shall sign and date the record.

(3) Assessment of AEs and SAEs

① Severity Grading

Grade 1: Mild; asymptomatic or slight; only clinical/diagnostic findings; no treatment required.

Grade 2: Moderate; requiring minor, local, or non-invasive treatment; limitation in instrumental activities of daily living appropriate for age.

Grade 3: Severe or medically significant but not immediately life-threatening; results in hospitalization or prolongation of hospitalization; disability; limitation in self-care activities of daily living.

Grade 4: Life-threatening; requiring emergency treatment.

Grade 5: Death related to the AE.

② Causal Relationship Judgment

The researcher assesses the potential causal relationship between AEs and the test product in accordance with the following classification criteria: a) reasonable temporal sequence between intervention initiation and AE onset; b) consistency of the suspected AE with known adverse reactions to the test drug/acupuncture; c) explainability of the suspected AE by concomitant medications, the patient's clinical status, or other therapies; d) resolution or alleviation of the AE after drug/acupuncture discontinuation; e) recurrence of the same reaction after re-administration/re-intervention. Based on these principles, causal relationships are classified into 6 levels: Definite, Probable, Possible, Unlikely, Unassessed, Unassessable.

Definite: Reasonable temporal sequence between intervention and reaction; reaction ceases or rapidly alleviates after discontinuation (some ADRs may persist for

days after discontinuation due to immune status); reaction recurs and worsens upon re-administration (positive re-challenge test); supported by literature, with exclusion of confounding factors such as underlying disease.

Probable: No re-administration, but otherwise consistent with "Definite"; or concomitant medications are present but essentially excluded as the cause of the reaction.

Possible: Close temporal relationship between intervention and reaction, supported by literature; but multiple drugs may be implicated, or progression of underlying disease cannot be ruled out.

Unlikely: Poor temporal correlation between intervention and reaction; inconsistent with known ADRs of the test product; similar manifestations may occur with underlying disease progression.

Unassessed: Incomplete report data, pending supplementation for assessment; or undetermined causal relationship due to lack of literature support.

Unassessable: Severe report omissions, undetermined causal relationship, and unobtainable supplementary data.

(4) SAE Reporting

Researchers shall closely monitor the occurrence of SAEs during the clinical trial. In the event of an SAE, the trial shall be terminated immediately, necessary measures taken to ensure subject safety, and the Ethics Committee and other relevant authorities notified within 24 hours.

16. Data Management

A clinical research coordinator, data manager/statistician, and clinical treating physician are appointed, ensuring separation of data managers, study designers, and clinical implementers.

Data Collection: Electronic Data Capture (EDC) system is used for data collection.

Data Recording: Original medical records and CRFs shall be completed truthfully and carefully as required; no content may be altered arbitrarily once entered.

If corrections are necessary for entry errors, the original record shall not be modified; only supplementary narratives may be used, signed and dated by the responsible treating physician.

Data Query and Correction: All observed results and abnormal findings in the clinical trial shall be promptly verified and recorded to ensure data reliability.

All instruments, equipment, reagents, standards, etc., used for various examinations in the clinical trial shall have strict quality standards and be used in normal working condition.

17. Statistical Analysis

After completion of the trial protocol and CRFs, a professional statistician develops a statistical analysis plan. A statistical analysis report is provided upon completion of data analysis.

(1) Statistical Analysis Software

Statistical analysis is performed using SAS 9.4 software.

(2) Basic Principles of Statistical Analysis

Statistical analysis includes descriptive statistics and inferential statistics. Baseline data are first described systematically and between-group balance tested, followed by intra-group and inter-group comparisons of outcome measures. Corresponding statistical methods are adopted for different types of outcome measures (binary, continuous, ordinal). Continuous indicators are described by mean, standard deviation, median, minimum, maximum, and interquartile range. Categorical indicators are described by case numbers and percentages. Ordinal categorical indicators (ordinal indicators) are described using both continuous and categorical variable methods.

(3) Missing Data Imputation

All missing data during the trial are handled using the Last Observation Carried Forward (LOCF) method. No outcome measure data are excluded unless otherwise specified.

(4) Baseline Data Analysis

Baseline demographic indicators (age, gender, ethnicity, BMI, etc.) and clinical baseline indicators (disease course, baseline OSDI score, FNGS 2.0 score, TMH TBUT, etc.) are statistically described:

Continuous data: "mean ± standard deviation" for normal distribution; median (interquartile range) for non-normal distribution;

Binary/count data: frequency (constituent ratio, %);

Ordinal data: frequency (constituent ratio, %).

(5) Efficacy Analysis

① Primary Outcome Measure

In the Full Analysis Set (FAS) and Per-Protocol Set (PPS), the number of responders, total enrolled subjects, and response rate of the IA group and SIA group are described by frequency (constituent ratio, %). The distribution of "≥50% reduction in OSDI score" and "<50% reduction in OSDI score" between the two groups is presented in a contingency table.

Chi-square test is used for inferential statistics to compare between-group differences in response rates and analyze the overall effect of IA.

Baseline Adjustment Analysis: If baseline OSDI scores are unbalanced between groups ($P \leq 0.10$), binary logistic regression analysis is performed with baseline OSDI score as a covariate to compare adjusted between-group response rates, calculating Odds Ratios (OR) and 95% Confidence Intervals (CI).

② Secondary Outcome Measures

Statistical analysis is performed separately for continuous and ordinal indicators, with all analyses conducted in both FAS and PPS.

Continuous indicators (TMH, TBUT, width of palpebral fissure incompleteness, FNGS 2.0 score): Described by "mean ± standard deviation"; median (interquartile range) for non-normal distribution, with minimum and maximum values reported. Paired t-test (normal distribution)/Wilcoxon signed-rank test (non-normal distribution) is used for intra-group pre- vs. post-treatment comparisons; independent samples t-test/Wilcoxon rank-sum test for inter-group comparisons; repeated measures ANOVA for multi-time point trends.

Ordinal indicators (meibomian gland analysis): Described by frequency (constituent ratio, %) for grade distribution and baseline improvement rate at each visit in each group. Wilcoxon signed-rank test is used for intra-group pre- vs. post-treatment comparisons; Kruskal-Wallis H test for inter-group comparisons; ordinal logistic regression for confounding factor adjustment.

(6) Safety Analysis

The type, frequency, and causal relationship with the test drug of AEs are described. Special notation is made for cases withdrawing from the study due to AEs and those with severe or serious AEs.

18. Quality Control and Quality Assurance

(1) Development of Standard Operating Procedures (SOPs)

Prior to trial initiation, researchers and the Contract Research Organization (CRO) jointly develop SOPs for the clinical trial to standardize operational methods, judgment criteria, and recording formats, ensuring strict adherence to the protocol by researchers.

(2) Investigator Training and Authorized Role Allocation

Prior to trial initiation, the principal investigator assembles a study-matched team including physicians, nurses, coordinators, etc.

Before study start-up, the principal investigator trains all medical staff participating in the trial on the clinical trial protocol, trial manual, SOPs, special precautions, etc. If project procedures are modified during the trial, relevant re-training is organized. True and complete training records are retained.

The principal investigator authorizes role allocation for relevant personnel, who shall perform duties in accordance with the authorization roster. During the trial, the principal investigator may add, remove, or adjust personnel and roles based on actual conditions, with updated authorization rosters. All personnel receive adequate training prior to performing operations.

(3) Document and Specimen Management

No biological specimens are collected in this study; only standardized management of all study documents and retained samples of key consumables is implemented. Study documents are stored in dual electronic and paper files: paper files in dedicated locked filing cabinets, electronic files encrypted and backed up regularly. All documents are completed standardly and traceably, with approval and registration procedures for borrowing and transfer. Retained samples of study consumables (intradermal acupuncture, acupuncture needles, etc.) are stored by batch with ledgers and classified in accordance with storage requirements, managed by dedicated personnel. Unused retained samples are disposed of in accordance with medical waste regulations after study completion, with complete records for future reference.

(4) Subject Compliance Management

Researchers will actively implement follow-up measures to control the case dropout rate within 10%.

19. Ethical Considerations

This clinical trial must be conducted in compliance with the Declaration of Helsinki and relevant Chinese clinical trial regulations. Prior to trial initiation, the clinical trial protocol, informed consent form, and other documents shall be submitted to the Ethics Committee for approval; the trial may be implemented only after approval. Modifications to the clinical trial protocol, informed consent form, and other documents during the study shall be approved by the Ethics Committee before implementation. Researchers shall ensure the rights and safety of subjects and protect their privacy.

20. Study Schedule

This is a single-center randomized controlled clinical trial of IA treatment for OSD after IFP, with an expected total study duration of 20 months. The timeline for each phase is closely integrated with the study flow, with specific scheduling detailed

below (all time points are based on the approval of the study protocol as the starting baseline):

(1) Study Initiation

Within 1 month after Ethics Committee approval of the protocol at Zhejiang Provincial Hospital of Traditional Chinese Medicine, all start-up work (study team training, procurement and acceptance of study supplies, EDC system debugging, blinding preparation, etc.) shall be completed, and the study officially initiated.

(2) Subject Enrollment Period

Subject recruitment commences immediately after study initiation, with a 12-month enrollment period. Recruitment and randomization of all subjects meeting inclusion/exclusion criteria shall be completed, ensuring standardized enrollment and complete baseline data.

(3) Completion of Intervention and Follow-up

Subjects receive 4 weeks of intervention treatment and 6 weeks of observation follow-up per the protocol. Intervention, visit assessments, AE recording, and follow-up data collection for all subjects shall be completed within 10 weeks after enrollment of the last subject, and the EDC data collection portal shall be closed.

(4) Data Management and Locking

Within 1 month after follow-up completion, all study data verification, query resolution, and missing data handling shall be completed. Data locking and unblinding shall be performed jointly by the principal investigator and statisticians.

(5) Statistical Analysis

Within 1.5 months after data locking and unblinding, the statistical team completes data analysis in accordance with the pre-specified statistical analysis plan and provides a statistical analysis report.

(6) Study Summary and Manuscript Preparation

Within 1.5 months after completion of the statistical analysis report, the principal investigator leads the study team in completing the study summary report, sorting out study results, conclusions, and clinical significance, and initiating academic manuscript preparation.

(7) Manuscript Submission and Publication

Within 2 months after completion of the manuscript draft, manuscript revision and internal peer review shall be completed. The manuscript is submitted to core journals in the fields of integrated traditional Chinese and Western medicine, acupuncture, and ophthalmology based on the study's findings, with target completion of external review, revision, and acceptance within 3 months after submission.

Reasonable buffer periods are reserved for overlapping phases of the study to ensure full implementation of quality control. All scheduling may be adjusted slightly based on actual study conditions after Ethics Committee approval, with timely notification to all study personnel upon adjustment.

【Single-Center Randomized Controlled Clinical Trial of Intradermal Acupuncture Intervention for Ocular Surface Disease Secondary to Intractable Facial Paralysis】Informed Consent Form

Part I: Informed Consent Information Sheet

Dear Study Participant,

You are cordially invited to consider participating in a clinical research study entitled " **Single-Center Randomized Controlled Clinical Trial of Intradermal Acupuncture Intervention for Ocular Surface Disease Secondary to Intractable Facial Paralysis"** . This study will be conducted at the First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Traditional Chinese Medicine), under the supervision of Binyan Yu (Associate Chief Physician).

Before you decide whether to participate in this study, please read the following content carefully. It will help you understand the purpose, procedures, potential benefits, risks, and discomforts of this study. If you have any questions, please consult the study doctor or research staff, who will provide you with detailed explanations. You may also discuss this with your family and friends before making a decision.

1. Research Background and Objectives

Intractable facial paralysis generally refers to peripheral facial paralysis that shows no significant recovery after conventional treatment. Clinical manifestations often include deviation of the mouth and eye, incomplete eye closure, synkinesia of facial muscles, and muscle contracture on the affected side. This condition usually results from severe facial nerve injury, or delayed, prolonged, or inappropriate initial treatment of peripheral facial paralysis. Peripheral facial paralysis, also known as peripheral facial palsy, falls under the categories of "Kou Pi" (facial paralysis) and

"Deviation of Mouth and Eye" in traditional Chinese medicine. It is commonly caused by exposure to cold, viral infection, and other factors leading to inflammation, acute edema, and compression of the facial nerve within the stylomastoid foramen. Bell's palsy is the most representative type, accounting for approximately 95% of clinical peripheral facial paralysis cases. About 1 in 60 people will develop Bell's palsy at some stage in life, with an annual incidence of 11.5–53.3 cases per 100,000 people. Studies show that 60%–87% of patients with intractable facial paralysis fail to recover completely and develop sequelae or permanent paralysis.

Due to severe facial nerve damage and a long recovery period, intractable peripheral facial paralysis is frequently accompanied by various ocular surface diseases. Incomplete eyelid closure, epiphora, and ocular motility disorders are the most common, which may lead to exposure keratitis, conjunctivitis, and even vision loss, severely affecting patients' daily work. Electronic devices have become essential for work, study, and social life in modern society, and patients cannot avoid using them, which further aggravates ocular injury. Meanwhile, frequent use of electronic devices leaves no time for damaged corneal epithelium to repair, turning intermittent ocular surface damage into persistent damage. Currently, there are no clearly recommended medications for peripheral facial paralysis in recovery phase guidelines. For related ocular surface diseases, symptomatic and supportive treatments such as sodium hyaluronate eye drops are commonly recommended. However, long-term corneal exposure combined with electronic device use limits the clinical efficacy of artificial tears for these patients. Therefore, exploring an effective, safe, convenient, and sustained treatment method is of great clinical value to resolve persistent ocular problems during facial paralysis.

Acupuncture is a treasure of traditional Chinese therapy. Studies show that electroacupuncture and other treatments effectively improve clinical symptoms in patients with dry eye syndrome, but they require high operator skill, are difficult for patients to adhere to, and have short-lasting effects. As an important part of acupuncture therapy, intradermal acupuncture stimulates acupoints gently and

continuously to regulate meridian Qi and blood and improve visceral functions. It features good efficacy, simple operation, minimal trauma, and high safety. A literature review reveals few high-quality clinical studies on intradermal acupuncture for ocular surface disease secondary to intractable peripheral facial paralysis. Preliminary pilot experiments by our research team indicate that intradermal acupuncture effectively improves OSDI scores in such patients. To further verify the efficacy and safety of this treatment, we will conduct a single-center, randomized, single-blind, placebo-controlled parallel trial. We aim to provide a convenient, safe, and widely applicable treatment for ocular surface disease secondary to intractable peripheral facial paralysis. This method is easy to implement, suitable for primary medical institutions and home rehabilitation, helps reduce medical burdens for both institutions and patients, and has important practical value and promotion prospects.

Study Objectives:

To preliminarily evaluate the effective rate of intradermal acupuncture intervention for ocular surface disease secondary to intractable facial paralysis via a single-center, randomized, single-blind, placebo-controlled parallel trial, and to provide a new effective treatment for ocular diseases after intractable peripheral facial paralysis.

To assess whether intradermal acupuncture synergistically improves ocular symptoms, restores ocular surface function, and promotes facial nerve recovery, and to clarify the feasibility, safety, and patient acceptance of intradermal acupuncture intervention, providing an optimized clinical treatment protocol.

This study has been reviewed and approved by the Ethics Committee in accordance with the principles of the Declaration of Helsinki and medical ethics.

2. Who Is Eligible to Participate?

(1) Diagnostic Criteria

Diagnostic Criteria for Peripheral Facial Paralysis: Main manifestations include paralysis of facial expression muscles, disappearance of forehead wrinkles on the

affected side, paralysis of the orbicularis oculi muscle, incomplete or unable eye closure, flattened nasolabial fold, drooping mouth angle, deviation of the mouth to the unaffected side when showing teeth, and food retention between the teeth and cheek on the affected side during mastication.

(2) Inclusion Criteria

1. Aged 18–65 years, male or female.
2. Meet the diagnostic criteria for peripheral facial paralysis; disease duration ≥1 month and ≤1 year; Facial Nerve Grading System 2.0 score ≥15; ratio of maximum CMAP amplitude of bilateral facial nerves (zygomatic branch/ocular branch) on electroneurography ≤20%.
3. Have at least one subjective ocular symptom (dryness, foreign body sensation, burning sensation, fatigue, discomfort, redness, fluctuating vision) AND Ocular Surface Disease Index (OSDI) score 30–80.
4. Voluntarily sign the informed consent form and be able to comply with treatment and follow-up.

(3) Exclusion Criteria

Patients meeting any of the following will be excluded:

1. Complicated with other underlying ocular diseases (glaucoma, keratitis, retinopathy, etc.) or acute inflammation/pathological conditions of the conjunctiva, sclera, eyelid, or cornea.
2. Underwent intraocular surgery or laser treatment within 90 days.
3. Systemic or topical use of antibiotics or drugs affecting tear secretion within 3 weeks; use of dry eye medications within 2 weeks.
4. Lacrimal passage obstruction, dacryocystitis/stenosis of nasolacrimal duct (positive Jones test); occluded lacrimal punctum or inability to close the eye completely due to damage to the nerve reflex arc.
5. Coagulopathy (thrombocytopenia, coagulation factor deficiency, etc.) or skin damage/infection at the intervention site.

6. Allergy to intradermal acupuncture materials (stainless steel, medical adhesive tape).
7. Pregnant or lactating women.
8. Severe heart, liver, or kidney disease, mental illness, or malignant tumor.
9. Participation in another clinical study within 1 month.

3. What Will You Do If You Participate?

1. Study Flow: If you agree to participate, the entire study will last approximately 10 weeks (4-week intervention period + 6-week observation/follow-up period).
2. Visits: You will have 6 study visits. During visits, you may undergo examinations including electroneurography (ENoG), ocular surface function tests, measurement of incomplete palpebral fissure closure width, and assessments using the Facial Nerve Grading System 2.0 and Ocular Surface Disease Index (OSDI) questionnaire.
3. Group Assignment: This study uses a randomized, double-blind, placebo-controlled design. You will be randomly assigned to one of two groups:

Experimental Group: Receive intradermal acupuncture intervention.

Control Group: Receive sham intradermal acupuncture intervention.

You will not know which group you are in. Unblinding can be performed rapidly in case of emergency.

Required Cooperation: You must use medications as instructed by the study doctor, truthfully record your feelings and any discomfort, attend all visits on time, and inform us of any changes in your health during the study.

4. Potential Benefits of Participation

1.Personal Benefits: You may directly benefit from the study intervention, such as significant improvement in uncomfortable symptoms of ocular surface disease secondary to intractable peripheral facial paralysis (epiphora, ocular foreign body

sensation, eye fatigue, etc.). You will also receive closer medical attention and examinations.

2.Social Benefits: Your participation will help the medical community better understand the efficacy and safety of intradermal acupuncture intervention for ocular surface disease secondary to intractable peripheral facial paralysis, providing potential treatment options for more patients in the future.

5. Potential Risks, Discomforts, and Adverse Reactions

1.Treatment-Related Risks: All treatments carry risks. Interventions such as acupuncture and eye drops used in this study may cause bleeding, hematoma, fainting, pain at the needle site, or mild infection at the puncture site. Although most adverse reactions are mild and transient, rare but serious adverse reactions cannot be completely ruled out. If any of the above occur, promptly inform your attending physician, who will evaluate and provide appropriate medical care.

2.Study Procedure-Related Risks: Ocular surface function tests required for the study may cause transient discomfort or mild pain.

3.Privacy Breach Risk: We will strictly protect your personal information and medical records, but a minimal risk of privacy breach remains.

6. Compensation for Study-Related Injury

If your health is harmed as a direct result of participating in this study, the First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Traditional Chinese Medicine) will bear corresponding medical expenses and provide financial compensation in accordance with relevant national laws and regulations. This will not affect your other legal rights. You are not required to waive any legal rights to sign this informed consent form.

7. Study-Related Costs and Compensation

1. Costs: All study-related costs for disposable intradermal acupunctures, disposable acupuncture needles, and study medications will be covered by the research team (or study sponsor).

2. Compensation: You will receive high-quality medical services during the study, including priority registration and free consultations, to compensate for your time and effort.

8. Voluntary Participation and Withdrawal

Participation is completely voluntary. You may refuse to participate or withdraw from the study at any time for any reason after signing the informed consent form. This will not affect your relationship with your doctor or your future medical care, and you will not face discrimination or retaliation.

The study doctor may terminate your participation if: the study is terminated early; you develop a condition unsuitable for continued participation; or you fail to comply with the study protocol.

9. How Is Your Privacy Protected?

Your medical records (study charts, laboratory reports, etc.) will be stored at the hospital as required. All information related to this study will be kept strictly confidential. Your identity will not appear in any public reports or publications. Only authorized personnel (researchers, Ethics Committee, drug regulatory authorities) may access your data within the scope permitted by law.

10. Additional Information

You may consult your study doctor at any time during the study with any questions.

If you have questions about your rights as a study participant or believe your rights have been violated, you may contact the Ethics Committee Office, which protects the rights and welfare of study participants.

Ethics Committee Office Contact: First Affiliated Hospital of Zhejiang Chinese Medical University Ethics Office, Tel: 0571-87072953.

Part II: Informed Consent Signature Page

Study Participant Statement

I have read the above information about this study. The study doctor has provided a full explanation and answered all my questions. I understand the purpose, procedures, potential benefits, risks, and discomforts of the study. I know participation is voluntary and I have the right to withdraw at any time without discrimination or retaliation.

I consent to the collection and use of my health information by researchers at the First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Traditional Chinese Medicine) for this study.

I voluntarily agree to participate in this study and will follow the instructions of the study doctor to the best of my ability.

Study Participant Signature: _____

Phone Number: _____

Date:_____

Legal Representative Statement (If Applicable)

I have read the above information about this study. The study doctor has provided a full explanation and answered all my questions. I understand the purpose, procedures, potential benefits, risks, and discomforts of the study. I know participation is voluntary and I have the right to withdraw the participant at any time without discrimination or retaliation.

I consent to the collection and use of the participant's health information by researchers at [Insert Institution Name] for this study. I approve the participant's enrollment in this study.

Legal Representative Signature: _____

Relationship to Participant: _____

Phone Number: _____

Date: _____

Researcher Statement

I confirm that I have explained the details of this study, including participants' rights, potential benefits, risks, and discomforts, to the participant and/or legal representative, and answered all their questions.

Researcher Signature: _____

Phone Number: _____

Date: _____

Study Doctor Contact Information:

Name: _____

Phone: _____

Important Note: Both you and the researcher will keep one signed copy of this informed consent form.

Ethics Approval Document

(Scientific Research Project)）

Approval No.2026-KLS-167-01

Initial Review Date	2026-04-01	Re-review Date	/
Review Venue	Conference Room No. 2, Administrative Building		
Project Number	/		
Clinical Research Project	A Single-Center Randomized Controlled Trial of Intradermal Acupuncture Intervention for Ocular Surface Diseases After Intractable Facial Paralysis		
Project Source	Self-funded Project (No Grant Funding)		
Review Documents	1.Initial Review Application (Scientific Research Project) 2.National Medical Registration System Application (2026.03.19, V1.0) 3.Clinical Research Protocol (2026.03.15, V3.0) 4.Informed Consent Form (2026.03.20, V3.0) 5.Study Medical Records and/or Case Report Forms, Subject Diary Cards and Other Questionnaires (2026.03.17, V3.0) 6.Professional Curriculum Vitae of the Principal Investigator (2026.03.16, V1.0) 7.List of the Research Team and Their Professional Curriculum Vitae (2026.03.16, V1.0) 8.Conflict of Interest Statement (2026.03.17, V1.0) 9.Research Qualification Certificate of the Principal Investigator (2026.03.17, No.20261160) 10.Letter of Commitment that Samples Shall Be Used Exclusively for This Project (2026.03.17, V1.0)		
Lead Unit	The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Traditional Chinese Medicine)		
Local Center	The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Traditional Chinese Medicine)		
Principal Investigator	Binyan Yu		
Ethics Review Method	☑ Full Committee Review　　□ Expedited Review		
Review Comments	Review Result: ☑Approved　　□Disapproved Upon review by the Ethics Committee, the research protocol is scientifically and rationally designed, with adequate protection for subjects, ensuring the security of personal information and the confidentiality of privacy. The conduct of clinical research for this project is hereby approved. During the research process, in the event of serious adverse events and unexpected events that affect the risk-benefit ratio of the research, a written report must be submitted to the Ethics		

	Committee of our hospital within the specified time limit.
Validity Period of Approval	12months
Frequency of Continuing Review	12months
Signature of Chairperson	
Ethics Committee of The First Affiliated Hospital of Zhejiang Chinese Medical University	
	Date：2026-04-01