Far Eastern Memorial Hospital
Informed Consent Form

You are invited to participate in this study. This form provides you with information about this study. The principal investigator or research team will explain the study to you and answer any questions you may have. Participation in this study is entirely voluntary. Your decision to participate or not will not affect your existing rights.

- Research Title: Effects of individualized exercise intervention combined with manual therapy on musculoskeletal system, cardiopulmonary endurance and quality of life in severe hemophilia patients with polyarthropathy.
- Principal Investigator: Wan-Jung Kao / Title: Physical Therapist
  Co-Investigator: Hui-Hsun Tien, Ting-Wei Chi / Title: Physical Therapist
  Contact Person: Wan-Jung Kao / Contact Number: 886-980908578
  Performing Unit: Rehabilitation Department
  Sponsoring Unit / Pharmaceutical Company: None
  Subject Name: / Medical Record Number:

I. Research Objectives:

The main clinical manifestations of hemophilia are muscle and joint bleeding, and the degeneration caused by recurrent bleeding is called hemophilic arthropathy. Past literature has found that manual therapy or exercise intervention can improve muscle strength, balance, cardiopulmonary fitness and enhance quality of life in hemophilia patients, but research has rarely focused on cases with multiple joint diseases. The purpose of this study is to investigate the effects of individualized physical therapy combined with manual therapy and exercise intervention on joint bleeding status, pain, range of motion, muscle strength, cardiopulmonary endurance and quality of life in severe hemophilia patients with polyarthropathy. This study aims to investigate the impact of individualized physical therapy combined with manual therapy and exercise intervention on joint bleeding episodes, pain, range of motion, muscle strength, cardiopulmonary endurance, and quality of life in severe hemophilia patients with polyarthropathy.

II. Research method and procedure:

A. Selection criteria and number of subjects:

1. Number of subjects: 10 subjects are expected to be admitted.
2. Inclusion criteria:
   a. Over 20 years old and diagnosed with severe hemophilia
   b. People who receive prophylaxis regularly
   c. There are more than 2 target joints (arthrosis)
3. Exclusion criteria:
   a. Unable to sign the informed consent form

b. Any neurological disease or major musculoskeletal system disease (such as fracture) one year ago
c. Have had more than 3 (exclusive) joint replacement surgeries (different joints)
d. Inability to walk due to hemophilic arthropathy or any other disease
e. Major bleeding events that pose risks or hinder research
f. Inability to follow instructions due to cognitive impairment

4. Recruitment method: through the Rehabilitation Department of Far Eastern Memorial Hospital, the Hemophilia Center and relevant hemophilia associations. Recruitment is open and a promotional leaflet has been given.
5. Method of consent of research subjects: After the assessment and confirmation of inclusion and before the start of the research, fully inform the experiment content and process, and ask the subjects to sign the human clinical trial consent form.

B. Research conduct method:

1. The physical therapists of the research team will evaluate whether they meet the inclusion criteria to recruit subjects who meet the conditions of this trial.
2. Fully inform the experiment content and process, and ask the subjects to sign the subject informed consent form.
3. Study location: Rehabilitation department
4. The execution content is as follows:
   a. Manual treatment: including fascia release, progressive passive stretching, joint mobilization, etc., and adjustments will be made according to the subject's current condition.
   b. Exercise therapy: including upper and lower limbs muscle strengthening, trunk(spine) exercise, and adjustments based on the subject's current condition.
5. Intervention schedule: Once a week for three months (about 12 weeks), 30 minutes of traditional physical therapy plus 30 minutes of individualized physical therapy intervention, about 1 hour.
6. Questionnaires and scales were conducted before intervention, at the 6th week after intervention (mid-term intervention) and at the 12th week (end of intervention) to evaluate changes in joint status, pain, cardiopulmonary endurance, functional level, and quality of life.
7. Subjects will be given NT$500 each in the 6th and 12th weeks respectively, for a total of NT$1,000 in traffic allowance.

III. The incidence, discomfort or danger of possible physical and mental side effects and the management:

Although the probability of occurrence is low, this study may still cause physical discomfort such as muscle soreness and joint bleeding due to this study. Therefore, before the test, people will be asked whether they receive prophylaxis regularly. If there

is any discomfort during the research, terminate immediately and deal with it appropriately. If discomfort occurs three times, the research project will be withdrawn early. During the execution of relevant intervention, professionals will assist in improving the safety maintenance of subjects.

IV. Expected research effects / expected benefits:

The aim of this study is to investigate the effect of individualized physical therapy, combined manual therapy and exercise intervention in severe hemophilia patients with polyarthropathy. According to past studies, manual therapy and exercise intervention effectively improve musculoskeletal conditions. It is hoped that in this study, the subject's pain, muscle strength, joint health, and cardiopulmonary endurance can also be improved, thereby enhancing the overall quality of life.

V. Other possible intervention options and descriptions:

Physical therapy is currently the safest and conservative choice for hemophilic arthropathy in hemophilia research and clinical practice. Therefore, this study is to investigate the combination of different physical therapy techniques in severe hemophilia patients with polyarthropathy, such as adding manual therapy and exercise intervention to improve pain, joint health, muscle strength and cardiopulmonary endurance, and at the same time prevent further bleeding. If you do not participate in this study, you can refer to the World Federation of Hemophilia's recommendations for other non-surgical treatments, for example 6-8 weeks of short-term prophyilaxis to control bleeding, selective COX-2 inhibitors, or surgical intervention.

VI. Other possible losses or benefits:

Rehabilitation effects may vary from person to person. During the intervention, the therapist will check the subject's condition and follow up regularly. Subjects who choose to participate in the trial may withdraw their consent and suspend participation in the study at any time. This decision will not affect the future medical care of the subject by the therapist. Please do not worry that withdrawal will affect future rehabilitation treatments.

VII. Damage Compensation and Insurance:

A. If adverse events occur and damage is caused in accordance with the human subject research plan established by this institute, Far Eastern Memorial Hospital shall be responsible for compensation. However, no compensation will be provided for the expected adverse events recorded in the informed consent form of subjects in this study.

B. In the event of physical or psychological adverse reactions, side effects or injuries caused by the plans set by this institute, this hospital and principal investigator will provide subjects with professional medical care and medical consultation. You do not have to pay for necessary medical treatment to treat adverse reactions or injuries.

C. Except for statutory compensation and medical care, this study does not provide other forms of compensation. If you are unwilling to accept such risks, please do not participate in the trial.

D. You will not lose any legal rights by signing this informed consent form.

E. This research was not covered by liability insurance.

VIII. Data retention period and storage method:

All data are collected and processed by the research team members. The paper data are locked in the personal cabinet by the principal investigator, and the electronic data are encrypted and stored on the personal computer in the office. After the research is completed, the research data will be kept for five years. After the expiration, the electronic data will be destroyed by the principal investigator. In addition, all paper copies of personal privacy information will be entrusted to Far Eastern Memorial Hospital to be burned and destroyed in the same way as paper medical records after the expiration of the period, to eliminate the risk of personal information outflow.

IX. If a subject withdraws from the study midway, the processing of personal data will be as follows:

Subjects have the freedom to choose to participate in the study and withdraw their consent midway through the study. If you choose to participate, you can also withdraw your consent and terminate your participation in the study at any time. This decision will not affect the medical care of you by the doctor. If you wish to discontinue your participation in the study for any reason, please contact the principal investigator Kao, Wan-Jung 886-980-908-578

How subjects' personal data will be processed after withdrawal (subjects please check one):

☐ Destroyed by Far Eastern Memorial Hospital

☐ Return

X. Subject rights:

A. Subjects will be given NT$500 each in the 6th week and 12th week respectively, for a total of NT$1,000 in traffic allowance.

B. During the research process, any significant findings related to your health or disease that may affect your willingness to continue to undergo human subject research will be provided to you immediately. If you have any questions about the study, you can also ask the contact person.

C. If you have questions about the nature of the research during the study process, have opinions about your rights as a patient, or suspect that you have been harmed by participating in the research, you can contact the Human Ethics Review Committee of our hospital to request consultation. The phone number is 886-2- 89667000 extension 2152 or the Human Research Protection Advisory Committee, whose telephone number is 886-2-89667000 extension 2546. To confirm the integrity of the informed consent

process, the committee may contact you by telephone during or after the study, and you have the right to refuse.

D. This consent form is made in duplicate. The principal investigator or our authorized personnel has given a copy of the consent form to you and has fully explained the nature and purpose of this study. The research team has answered your questions about this study.

XI. Confidentiality:

Far Eastern Memorial Hospital will treat your information as confidential to the extent regulated by law. You also understand that the health authorities and our hospital's Human Ethics Review Committee have the right to review your information and will abide by the ethics of confidentiality.

XII. Conflict of interest:

The funding for this study came from Far Eastern Memorial Hospital, so there is no issue of commercial interest.

XIII. Signature

A. The principal investigator, co-investigator or authorized researcher has explained and answered in detail the nature and purpose of the above-mentioned research methods in this research project, as well as the possible risks and benefits.

☐ Principal investigator / ☐ Co-investigator / ☐ Authorized researcher

Signature:_____ Date:_____

B. The subject or legal representative / person with consent rights has a detailed understanding of the above-mentioned research methods and the possible risks and benefits. Any questions about this research project have been explained in detail by the principal investigator, and they agree to accept them as voluntary participants in human subject research projects.

Subject Signature:_____ Date:_____

Date of birth: _____ / _____ / _____
Telephone:
National identity card unified number:
Mailing address:

*Participants need to know:

1. What is human subject research?

   "Research" is an investigation done to answer a question. "Research" and "treatment" are different.

   Participation in the research is not mandatory, so before participating in the research, you must clearly understand the following points: the purpose of the research, what will happen during the research process, what adverse reactions may occur, the personal benefits of the research trial, and the expected effects.

2. Human Ethics Review Committee

   This is a review unit established to ensure that human research is scientifically and ethically appropriate. It is composed of medical personnel with professional knowledge, as well as non-medical background people such as legal experts, social justice people or representatives of civil society groups, to assist researchers in understanding the situation of participants and ensuring the rights of participants. We will track the approved research projects and may contact you by phone to confirm the completeness of the consent form signing process.

3. Participants' rights and interests

   Be fully informed, freely decide whether to participate in the research, be able to ask questions about the research at any time, maintain privacy and confidentiality, retain the legal rights you currently have, and be treated with dignity at all times while participating in the research project, treat with respect.

   For more detailed information, please visit our website: https://www.femh-irb.org