Participant Informed Consent

Dear participants:

If your doctor thinks you have benign prostatic hyperplasia (BPH), we invite you to participate in this study aiming to evaluate the efficacy and safety of electroacupuncture (EA) for relieving lower urinary tract symptoms (LUTS) in men with BPH.

Before you decide to participate in the study, please read the following information carefully. It is helpful for you to know this study, understand why the study is performed, the study procedures, the duration and benefits of the study, risks, and potential discomforts during and after study participation.

If you like, you can also discuss this study with your relatives and friends, or consult doctors for explanation and help to make the decision.

I. Introduction

Benign prostatic hyperplasia (BPH) is a common disorder that affect about 36.6% of men aged over 40 years in China. In accordance with the guidelines of the European Association of Urology (EAU) and American Urological Association (AUA), options of the treatment to LUTS in men with BPH range from watchful waiting to medical and surgical interventions, depending on the severity of the symptoms and the level of discomfort, which however may cause side effects. Previous studies suggest that EA may be a potential treatment for BPH.

In this study, a randomized controlled trial design will be used and we aim to evaluate the efficacy and safety of EA for relieving LUTS in men with BPH. This study will be carried out simultaneously in 11 hospitals all over China, and we expect a total number of 306 participants for voluntary participation.

II. Inclusion and exclusion criteria

Participants will be included if they have:

(1) Diagnosis for LUTS attributed to BPH in accordance with the guidelines of EAU and AUA;

(2) Men aged between 40 and 80 years;

(3) LUTS due to BPH for at least 3 months;

(4) International Prostate Symptom Score total score ≥ 8;

(5) Prostate volume ≥ 20 mL;

(6) Maximum urinary flow rate (Qmax)≤ 15 mL/s;

(7) Voluntarily participate in the trial and sign the written informed content.

Participants will be excluded if they have:

(1) Post-void residual urine volume ≥ 150 mL;

(2) Acute urinary retention or catheterization within the 3 months;

(3) Prostate cancer or prostate-specific antigen level (PSA) ≥ 4.0 ng/mL;

(4) Neurogenic lower urinary tract dysfunction; prostatitis; urinary tract infections; urethral strictures; bladder diverticula; bladder stones; bladder cancer; history of genitourinary system surgery (prostate, bladder, urethra, etc.);

(5) Previous acupuncture treatment for BPH in the preceding one month, or usage of α-blockers, 5α-reductase inhibitor, muscarinic receptor antagonists, or any other specific medication in the previous two weeks unless a stable 5α-reductase inhibitor usage of over 3 months;

(6) Severe lung, heart, liver, kidney, metabolic, or mental illness, coagulation dysfunction, or with obvious cognitive dysfunction;

(7) Installed cardiac pacemaker, allergy to metal, severe fear of acupuncture or unbearable to the stimulation of EA.

III. What do you do next, if you decide to participate?

1. Before your enrollment in the study, your medical history will be collected and you will receive a series of examinations to determine whether you are eligible to participate in the study, including physical examination, transabdominal ultrasound, Qmax and PSA. You will also need to complete a series of questionnaires to assess the severity of the disease and the influence on quality of life.

2. If the results of the above screening examinations meet the inclusion criteria and you are willing to participate in this study, you will be invited to continue study participation in the following steps:

(1) Based on the random number generated from the computer, the doctor will assign you to either the traditional acupuncture or minimal acupuncture group. Participants in

the traditional acupuncture group will receive deep needling on the Ciliao (BL32), Zhongliao (BL33), Huiyang (BL35), and Sanyinjiao (SP6) for 30 min; participants in the minimal acupuncture group will receive minimally invasive, superficial needle insertion of 2-3mm on the corresponding acupoints.

(2) In the study, Hwato brand disposable needles (Suzhou Medical Appliance, Jiangsu, China, Jiangsu Food, Drug, and Medical Appliance Administration production approval No.20010020, Registration No:20162200970) will be used.

(3) The duration of this study is 33 weeks in total for a patient including 1-week baseline assessment, 8-week treatment, and 24-week follow up. Frequency and duration of acupuncture: 3 sessions per week in weeks 1-8. The participants will receive 24 sessions of treatment in total.

(4) During the study period, you need to complete the questionnaires faithfully.

3. Other requirements for your cooperation

As a participant of this study, you will have some relevant responsibilities, such as adherence to the schedule for examination, treatment, and clinical follow-up. In addition, you are also responsible for reporting any changes in your physical and mental status to your doctor during the study process regardless of whether you think these changes are related to the study or not. You should follow the scheduled appointments with the doctor to come to the hospital for treatment. Your follow-up is very important because the doctor will determine whether the treatment that you are receiving really works and their safety profile.

During the study, you are not allowed to use other treatments for BPH. However, for intolerable symptoms, medication use such as α-adrenergic blockers is allowed, as long as it is recorded accordingly, including the name and the dosage of the medication use.

IV. Potential benefits of study participation

You may benefit from this study. The benefits may include improvement of symptoms, even by minimal acupuncture. The study may also help doctors and researchers to further evaluate the efficacy and safety of EA for relieving LUTS in men with BPH. The information will be beneficial in the management of other patients with a similar condition in the future. If you decide to participate in the study, you will get relevant

physical and biochemical examination as well the study intervention for free during the study period.

V. Potential side effects, risks, discomforts, and inconveniences

The doctors will make every effort to prevent and treat any side effects brought on by this study. During treatment, you may feel soreness, numbness, heavy, distension sensation, etc., which are normal reactions to acupuncture. EA treatment may have some adverse effects, but it is rare and mild. You may feel fainting due to your individual physique or emotional stress when receive acupuncture needling. Your symptoms should be relieved after the cessation of EA treatment and rest. Localized bleeding, hematoma, and other phenomena may occur after EA treatment, and these phenomena should disappear after applying local pressure. If infection occurs in the needle site, your doctor will handle it timely. With the treatment following the study protocol in the study, if you experience adverse reactions and events related to EA treatment, please feel free to call your doctor for help. The doctor will provide you timely treatment. If injuries have been confirmed and are caused by adverse reactions and events of the study, the study group will deal with them appropriately in accordance with relevant provisions. If you experience any discomfort or new change of your symptoms, or any other unforeseen circumstances during study period, regardless of whether these events are relevant with treatment of the study or not, you shall promptly notify your doctor, and he /she will evaluate the condition and give you appropriate medical treatment.

VI. Payments/compensation for participation

If you participate in the study, during the study, you will get relevant physical and biochemical examination and EA treatment for free. If adverse events occur during the study, they will be managed accordingly by medical experts who will also identify whether they are related to the study or not. The treatment and examination required for your concomitant diseases nonrelated to the study will not be free of charge.

VII. Confidentiality of personal information

All the information related to your participation in this study will be kept confidential by the institute where your participation takes place. Only the institutes responsible for

the study, clinical research institutes, and ethics committees may have access to your medical records. Your name will not appear in any publication or report related to this study. We will make every effort to protect the privacy of your personal medical information as per legal requirements and laws.

VIII. How to acquire extra information?

You can ask any questions about the study at any time and will get answers timely. If we notice any new information that may affect your willingness and decision to continue participating in the study, the doctor will keep you informed.

IX. Can you voluntarily choose to participate in or withdraw from the study?

Whether to participate in this study or not entirely depends on your desire. You can refuse to participate in the study, or withdraw from the study at any time during the study, which will not affect the relationship between you and your doctor and will not affect your medical interests or interests in other areas. For the consideration of your best interests, doctors or researchers may terminate your participation in this study at any time. If you withdraw from the study for any reason, you may be asked for information related of EA treatment or the use of other medications during your participation of the study. If the doctor considers it necessary, you may also be asked to have some laboratory tests and physical examinations performed.

X. What you need to do now?

Decide whether to participate in this study or not. Before you make the decision to participate in the study, please ask your doctor if you have any concerns.

Thank you for reading the above information. If you decide to participate in this study, please tell your doctor, he / she will help you make arrangement for the study.

Please keep this document for your own record.

Informed Consent: Signature Page

Study title: Electroacupuncture for lower urinary tract symptoms in men with benign prostatic hyperplasia: a randomized controlled trial

Organizer of this study: Guang'anmen Hospital, China Academy of Chinese Medical Sciences

Collaborative institute:

Statement of agreement:

I have read the above information about this study and have the opportunity to discuss this study with my doctor and ask questions. All my questions were answered satisfactorily. I understand the potential risks and benefits from participation in this study. I understand the participation of the study is voluntary and I confirm that I was given sufficient time for consideration of study participation. I confirm that I understand that:

I can always ask the doctor for additional/more information.

I can withdraw from the study at any time without discrimination or retaliation and my medical treatment and interests will not be affected.

I understand that if I withdraw from the study, I will tell the doctor the changes of my disease condition and complete the relevant physical and biochemical examinations if needed, which will be very helpful for the whole study.

If I need to take any other medications due to the changes of my medical condition, I will seek medical advice from the doctor beforehand or afterwards tell the doctor truthfully.

I agree to allow the research institute, collaborative institutes, and ethics committees to inspect the data relevant to my study participation.

I will receive a signed and dated copy of the informed consent form.

Finally, I decide and agree to participate in this study and ensure the adherence to doctor's orders to the best I can.

Signature of patient: Year month day

Telephone:

I confirm that I have explained this study in detail to the patient, including patient's rights as well as the potential benefits and risks, and have given the patient a signed copy of the informed consent form.

Signature of doctor: Year month day

Office phone number of doctor: