A prospective, randomized, controlled clinical trial:

The association between Weizhong point and waist based on infrared thermal imaging technology

Study type: Clinical study

Study Center: The Third Affiliated Hospital of Zhejiang Chinese Medical University

Department: Acupuncture department

Signature: Yi Liang

Date: 2022.10.10

The study will be conducted in accordance with this clinical study protocol and GCP

CONTENTS

I. Research Background

As one of the components of traditional medicine, acupuncture and moxibustion is widely used at home and abroad due to its exact curative effect and no toxic side effects. It has been widely accepted and used in 183 countries and regions around the world. However, the biological basis and intrinsic mechanism of acupuncture and moxibustion have not been fully explained, although high-quality papers have been published in succession. With the continuous innovation of life science research technology and the deepening of modern research on acupuncture and moxibustion, the mysterious veil of the effect law and mechanism of acupuncture and moxibustion has been gradually unveiled. For example, academician Han Jisheng and his team have applied neurobiological techniques to prove that there are differences in the analgesic effect and onset time of different frequencies of electroacupuncture. The intrinsic biological basis may be related[1-3] to the release of different types of central opioid peptides at different times and different parts promoted by different frequencies of electroacupuncture. Recently, Professor Ma Qiufu's team at Harvard University revealed the regional specificity of electroacupuncture stimulation by using biological technologies such as lentivirus technology and gene mice, and found that there were different biological bases for the anti-inflammatory effects of electroacupuncture at different depths and intensities. The research results were published in Nature and Neuron[4,5]. The international academic status of acupuncture has also been further improved. Therefore, the biological basic research of acupuncture and moxibustion plays a pivotal role in both the explanation of the mechanism of traditional acupuncture and moxibustion and the promotion of its further development.

The traditional theory of acupuncture and moxibustion is continuously summarized and refined based on the clinical practice experience of predecessors. Although the clinical efficacy is stable and widely used, there is still a lack of objective evidence and biological basic research. Therefore, on the basis of the summary of previous experience, it is particularly important to deeply reveal the intrinsic biological basis of the classic discussion of acupuncture and moxibustion through modern scientific research technology. In addition, although the human disease model is constructed through animal experiment simulation, a part of the therapeutic mechanism of acupuncture and moxibustion can be explained by comparing the physiological and biochemical indexes and functional indexes of the model animals in each group. However, the ideology and social attributes of human beings directly lead to insurable huge differences between human beings and animals. Therefore, clinical trials based on human beings are still an indispensable part.

It is mentioned in Neijing (The Classic of Internal Medicine) that Weizhong acupoint is used to treat waist diseases. It is recorded in Plain Questions: "The foot Taiyang pulse causes low back pain, citing the back of the neck ridge as the severe form, and needling it at Zhongtaiyang for severe bleeding". After the summary and summary of many doctors, the basic symptoms of Weizhong acupoint were refined as waist and leg[6] symptoms in the Song Dynasty, and then continued to summarize and summarize. Then, the "Wei zhong qiu" in the song of the four general acupoints in the Complete Compendium of Acupuncture and Moxibustion, which is still in use today. In clinical practice, bloodlet therapy[7], electroacupuncture[8], mo[9]xibustion and other methods are often applied at Weizhong point to treat various lumbar disorders, and good effects are obtained. The existing studies have preliminarily shown that there is some objective relationship between the waist and back and Weizhong point. For example, the stimulation of Weizhong point can observe the rich[10] local blood supply, the increase[11] of local temperature, and the improvement[12] of waist muscle fatigue resistance. When the waist and back lesions occur, acupoint sensi[13]tization phenomena such as force sensitivity, heat[14] sensitivity and local electrical resistance changes[15] can also be observed at Weizhong point. However, the specific association between Weizhong point and waist and back still needs to be further explored and improved. Therefore, this study intends to take the connotation study of "Weizhong acupoint on waist and back" as the entry point, to explore the correlation between the waist and Weizhong acupoint through infrared thermal imaging technology, and to explore the differences in the image of the waist observation area by different intervention methods, in order to provide some reference for the interpretation of its scientific connotation.

Ii. Main research content, objectives, program and progress, and key problems to be solved:

1. Research Content

The healthy people were selected as subjects and treated with moxibustion. FLIR E53 infrared thermal imager was used as the observation instrument to detect the dynamic changes of skin temperature in a specific area of the waist after different interventions (acupuncture

and moxibustion) at different acupoints (Weizhong point and Chize point), in order to further explore the relationship between the waist and Weizhong point. To provide an objective research basis for enriching the scientific connotation of "waist and back".

2. Objectives of the study

To explore the relationship between the waist and Weizhong points and whether acupuncture and moxibustion have different effects on the observation area of waist by observing the changes of local average temperature of waist in healthy subjects after applying acupuncture or moxibustion to different points.

3. Study PROTOCOL

The investigator clearly and orally explained the study and its potential risks and benefits to the subject before starting the study. After obtaining consent from the patient or his or her authorized person, the patient or his or her authorized person and the investigator signed and dated the informed consent form. Patients or their authorized persons could be screened for participation in the study only if they had provided written informed consent.

3.1. Study Protocol

Subjects were screened strictly according to the diagnostic criteria, inclusion criteria and exclusion criteria. After confirmation of enrollment, they were randomly divided into groups

according to the random number table until the total number of observation was completed.

Healthy subjects aged 18-40 years old from Zhejiang Chinese Medical University were included in this study.

3.1.1. Estimation of sample size

This project uses the sample size calculation method of 2×2 factorial design. Referring to the changes[10,16] of waist average temperature in previous similar experiments and the results of pre-experiments, the following assumptions are made:

- Acupuncture × Weizhong acupoint (right) group > moxibustion × Weizhong acupoint (right) group > all other groups
- Acupuncture × Weizhong (right) group > acupuncture × Chize (right) group
- Moxibustion method × Weizhong point (right) group > Moxibustion method × Chize point (right) group

Δ (℃) / Different points	Different interventions	
	Acupuncture	Moxibustion
Weizhong acupoint (right)	1.4	0.7
Chieze Cave (right)	0.3	0.2

Two-sided test was used without considering the interaction effect, and the number of samples required for each combination was estimated by comparing the means of two samples (see Medical Statistics edited by Sun Zhenqiu). The specific calculation formula was as follows, and the maximum value was selected as the minimum number of samples in each group:

$$n = 2\left[\frac{\left(u_\alpha + u_\beta\right) \times \sigma}{\delta}\right]^2 + \frac{1}{4}u_\alpha^2$$

$$N = max\left\{n_1, n_2, n_3\right\}$$

Where N is the required amount of samples; n_1 is the sample$_2$ size required for comparison between the acupuncture and moxibustion at the Weizhong acupoint group, the acupuncture and moxibustion at the Chize acupoint group,$_3$ the acupuncture and moxibustion at$_4$ the Chize

acupoint group, and the acupuncture and moxibustion at the Chize acupoint group. Because n_4 is not the key object of this study, it is not included in the calculation of sample size. $\delta=\mu_1-\mu_{,2}$ is the difference between the two population means,σ is the population standard deviation (assuming the two population standard deviation is equal); u_α and u_β are the values of u corresponding to the test level α and the type I error probability β, respectively.

At the significance level of $\alpha=0.05$ (two-sided), the test power $(1-\beta)=80\%$ was selected. According to the results of the preliminary experiment, we set $\sigma=1.17$, and the sample size was 45 / group, with a total of 180 cases in four groups.

3.1.2. A randomized controlled trial was designed and conducted

(1) Healthy subjects were randomly assigned by SPSS 20.0 software program. The 180 digits were randomly divided into a moxibustion group at Weizhong point, a moxibustion group at Chize point, an acupuncture group at Weizhong point and an acupuncture group at Chize point according to the ratio of 1:1:1:1. The grouping information was kept confidential by the project leader.

(2) The random allocation card was prepared as follows:

Association between Weizhong point and waist and back based on infrared thermal imaging technology
No. :
Groups:
Methods of intervention:

(3) The random assignment card is sealed in an envelope with the same number recorded

on the envelope as the card.

(4) Arrange the envelopes containing the randomization cards in order of number

(5) The randomization cards were made and kept by the investigators and distributed to the operators during the study. When eligible subjects entered the study, the operator opened the same numbered envelopes in the order in which they entered and grouped according to the rules of the cards inside the envelopes without making any changes. Participants in the group assignment did not participate in the statistical analysis of the data. Data extraction and statistics were collected and sorted by the personnel who did not know the grouping, and the researchers, operators, and statisticians were separated.

3.1.3. Inclusion criteria

① Age ≥18 years old, both sexes, 18.5≤BMI≤23.9 kg/m^2;

② Previous good health without organic diseases;

③ Understand the study process voluntarily participated in the study and signed the informed consent form.

3.1.4. Exclusion Criteria

① Women who are menstruating, pregnant, or breastfeeding;

② Unable to complete the filming in a prone position;

③ Those with skin diseases or skin damage, sensory disorders, scars or vegetations at

the test points;

④ Patients with serious systemic diseases, or those considered by the investigators to be unsuitable for the study;

⑤ Patients with epilepsy, head injury or other related neurological diseases.

3.1.5. Exclusion and expulsion criteria

Exclusion criteria (those who have been enrolled but meet one of the following criteria should be excluded) : (1) Those who do not meet the inclusion and exclusion criteria are found in the trial; (2) obvious adverse reactions occurred during the treatment; (3) The subjects were not treated according to the treatment plan after enrollment. Note: The excluded cases should be explained, and the original medical records should be kept for future reference. No statistical analysis of efficacy will be performed, but those who have received at least one treatment and have records can participate in the analysis of adverse reactions.

Drop-out criteria (patients who had been enrolled but had not completed the clinical protocol were considered drop-out in the following circumstances) : (1) patients withdrew or lost follow-up; (2) Serious adverse reactions or adverse events occurred during treatment.

Note: The reasons for dropouts should be explained, and the study medical records should be kept for future reference. Data were not carried forward at follow-up.

3.1.6. Termination criterion

(1) Specialists will be responsible for the evaluation of severe adverse reactions during the study to determine whether to continue or terminate the study;

(2) if the subjects developed serious complications or other serious diseases during the study period and needed to take emergency measures;

(3) the subjects could not continue the study for other reasons.

3.1.7. Adverse events

Adverse events and the reasons for dropouts were recorded in detail.

3.2. Interventions

In this study, the subjects were randomly divided into a moxibustion group at Weizhong point, a moxibustion group at Chize point, an acupuncture group at Weizhong point, and an acupuncture group at Chize point at a ratio of 1:1:1:1 for a randomized controlled trial to observe the relationship between waist and Weizhong point. Proposed research time: January 1, 2023 to December 31, 2023. Specific treatments are as follows.

3.2.1. Acupuncture at Weizhong acupoint group:

① Acupoint selection: Bilateral Weizhong (BL40)

② Location: Refer to the national standard of the People's Republic of China (GB/T 12346-2006) "Acupoint Name and Location"

③ Acupuncture operation: The acupuncture needles of φ25×40mm Huatuo brand were

selected and sterilized at Weizhong points with 75% alcohol. Acupuncture was performed avoiding the nerves and blood vessels. The depth of the needles was about 1 cun (33mm). When the subject had deqi sensation such as acid, numbness, and swelling pain, the manipulation was stopped, and the needle was retained for 30 minutes. No manipulation stimulation was given during the retention period.

④ The intervention time was 30 min

3.2.2. Acupuncture Chize acupoint group:

① Acupoint selection: Bilateral Chize (LU5)

② Location: Refer to the national standard of the People's Republic of China (GB/T 12346-2006) "Acupoint Name and Location"

③ Acupuncture operation: the same as Weizhong point operation.

④ The intervention time was 30 minutes

3.2.3. Moxibustion committee point group:

① Acupoint selection: bilateral Weizhong (BL40)

② Location: Refer to the national standard of the People's Republic of China (GB/T 12346-2006) "Acupoint Name and Location"

③ Moxibustion operation: the ambient temperature was controlled at 25-27℃, and the humidity was controlled at 40%-60%. The subjects were placed in the prone

position, with their right lower limb exposed, and intervention was applied to the Weizhong acupoint area with Fuyang moxibustion

④ The intervention time was 30 min

3.2.4. Moxibustion at Chize point group:

① Acupoint selection: Bilateral Chize (LU5)

② Location: Refer to the national standard of the People's Republic of China (GB/T 12346-2006) "Acupoint Name and Location" in 2006.

③ Moxibustion method operation: same as above

④ The intervention time was 30 minutes

3.2.5. Efficacy indicators and evaluation

(1) Baseline MEASURES: Through interviews and questionnaires, the subjects' gender, age, weight, height, frequency (weekly) of waist discomfort (such as waist acid, etc.), and whether they had received acupuncture/moxibustion related treatment were collected. Before the intervention, the average temperature of waist observation area (the geometric figure surrounding the second lateral line of bilateral bladder and the horizontal lines of T12 and S1) was recorded by infrared thermal imaging instrument.

(2) The main outcome measures were the average temperature changes in the waist

observation area (the geometric figure surrounded by the second lateral line of bilateral bladder and the horizontal lines T12 and S1) 30 minutes after the intervention and immediately after the intervention

(3) Secondary outcome measures:

① The highest temperature in the designated area of the waist 30min after applying the intervention;

② The average temperature change value of the designated area of the waist was measured 5 min and 15 min after intervention.

③ The average temperature of local acupoints (φ=2cm) at Weizhong and Chize before intervention and 30 min after intervention were recorded.

④ Evaluation of waist warm sensation: Binary data (yes/no) and NRS score (0-10) were used to record the waist warm sensation and its intensity during the intervention.

⑤ The differences of pain threshold before rest and immediately after the intervention were compared at Shen双shu (BL 23), Zhishi双 (BL 52), Mingmen (GV 4) and We双izhong (BL 40).

(4) Safety evaluation: the adverse reactions and their manifestations, occurrence time, degree, treatment measures, process and outcome were recorded, and the correlation

between the adverse reactions and the treatment was judged.

(5) Compliance evaluation: the drop-out situation and reasons were recorded and analyzed.

3.3. Emergency response

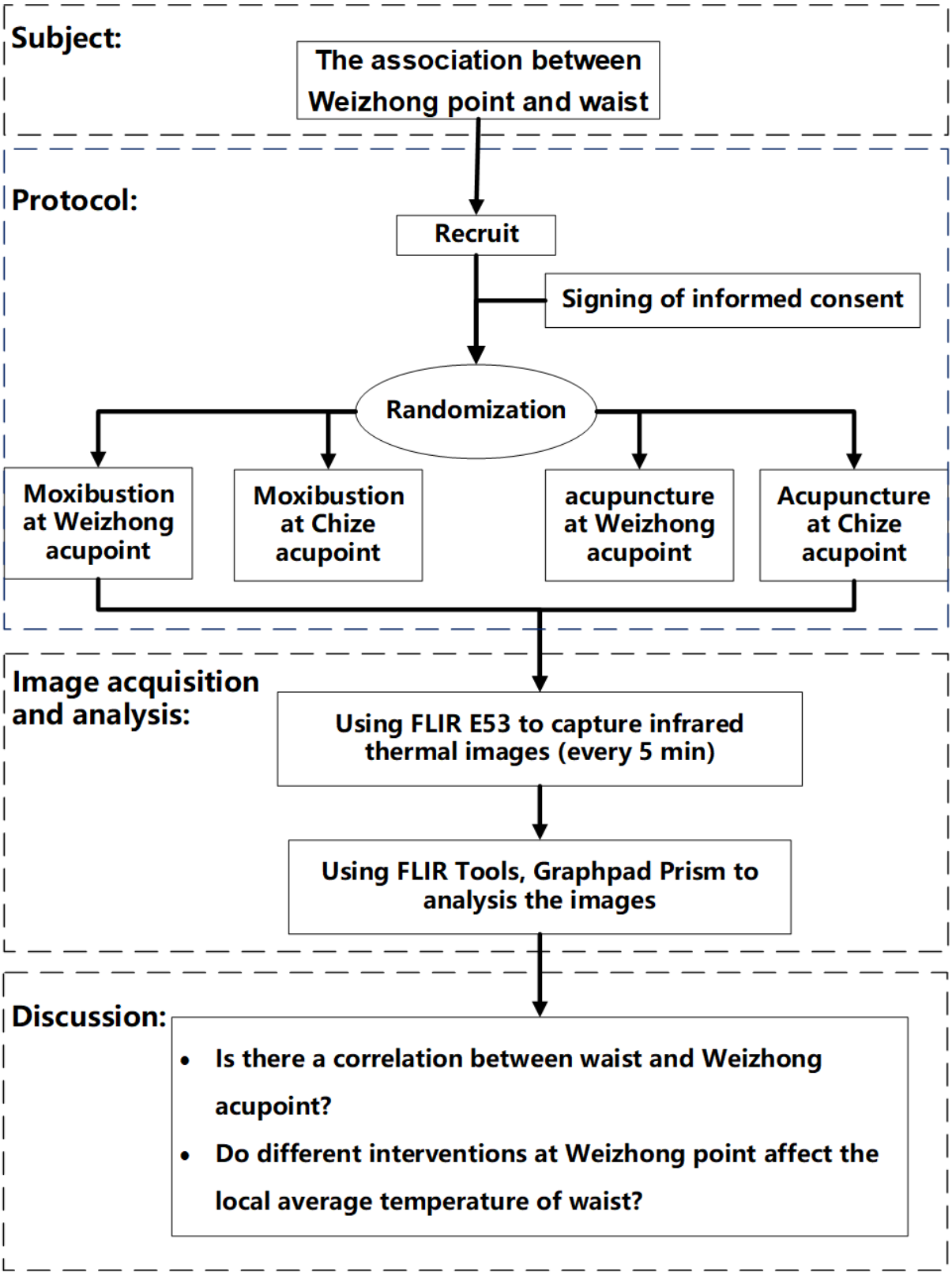
(1) Dizzy acupuncture/moxibustion: the intervention (acupuncture/moxibustion) should be stopped immediately, all the acupuncture needles should be removed, the patient should lie flat with the head slightly lower, unbutton his clothes, and pay attention to keep warm. If he lies still for a while, he can return to normal. On the basis of the above treatment, the severe cases can be treated with acupuncture at Shuigou (GV 26), Ciliao (BL 32), Neiguan (PC 6), Zusanli (ST 36), Yongquan (SP 9), etc., or moxibustion at Baihui (GV 20), Guanyuan (CV 4), Qihai (CV 6), etc. If the patient is still unconscious, breathing is weak, and the pulse is weak, first aid measures should be taken and emergency consultation should be requested.

(2) Burn injury: the intervention was stopped immediately, and the patients were rinsed with running cold water or applied with ice packs locally. If there were no blisters or small blisters, topical scald ointment was applied after disinfection with iodophor. If the scope of blisters is large, after disinfection, the blisters are broken by sterile syringes, and the liquid inside the blisters is drained, and then the sterile dressing is applied.

(3) Subcutaneous hemorrhage: if there is a small amount of subcutaneous hemorrhage

and local bleeding, no special treatment will be done. If the local swelling and pain is severe, the area of cyan is large and affects the activity function, cold compress is given within 24 hours to stop bleeding, and hot compress or local moxibustion is given after 24 hours to promote the stasis to dissipate and absorb.

3.4. Technical route



Iii. Adverse events (described according to the subject)

1. Definition of adverse events

From the time the subject signed the informed consent to the end of the intervention, events closely related to the intervention occurred, including the following:

-- Acupuncture/dizzy moxibustion

-- Burn and scald

-- Subcutaneous bleeding

2. Information on adverse events was obtained

The basic information of the acupoint area and all adverse events reported by the subjects during and after the intervention were observed by the research doctors.

3. Adverse events were observed and recorded

Any symptoms and signs that occurred from the beginning of the intervention to the end of the intervention were closely related to the intervention method, such as dizzy/dizzy moxibustion, burn and scald, subcutaneous hemorrhage, etc.

4. Management of adverse EVENTS

(1) Dizzy acupuncture/dizzy moxibustion: stop the intervention (acupuncture/moxibustion) immediately, and remove all the acupuncture needles, make the patient lie flat with the head slightly lower, unbutton his clothes, and pay attention to keep

warm. If he lies still for a while, he can return to normal. On the basis of the above treatment, the severe cases can be treated with acupuncture at Shuigou (GV 26), Ciliao (BL 32), Neiguan (PC 6), Zusanli (ST 36), Yongquan (SP 9), etc., or moxibustion at Baihui (GV 20), Guanyuan (CV 4), Qihai (CV 6), etc. If the patient is still unconscious, breathing is weak, and the pulse is weak, first aid measures should be taken and emergency consultation should be requested.

(2) Burn injury: the intervention was stopped immediately, and the patients were rinsed with running cold water or applied with ice packs locally. If there were no blisters or small blisters, the patients were locally sterilized with iodarone and then broke through the burn ointment. If the range of blisters was large, sterile syringes were used to break the blisters after disinfection, and sterile dressings were used to bandage the blisters after removing the liquid in the blisters.

(3) Subcutaneous hemorrhage: if there is a small amount of subcutaneous hemorrhage and local bleeding, no special treatment will be done. If the local swelling and pain is severe, the area of cyan is large and affects the activity function, cold compress is given within 24 hours to stop bleeding, and hot compress or local moxibustion is given after 24 hours to promote the stasis to dissipate and absorb.

4. Ethics and quality

Prior ethics committee approval will be obtained before the start of this study.

It was important to obtain authorization for the use of the data before enrollment. To protect patient privacy, patient initials will be recorded on the CRF.

5. Data management

Investigators were required to fill in the collected data into the case report form and collect or record the data in EXCEL according to the requirements of the study protocol. Zheng Siyi was responsible for data management to ensure the authenticity, completeness and accuracy of the clinical trial data. At the end of the study, case report forms of all enrolled patients will be submitted to the data management center by the investigator. These case report forms should be completed and signed. Case-report form data collected from the sites will be checked for consistency, and question forms will be issued for inconsistent data, requiring investigator clarification.

6. Statistical analysis

1. Statistical software

The data were analyzed by a third party statistician who was not involved in the preliminary study. Statistical software (SPSS 26.0) was used for statistical analysis.

2. Description of data

Measurement data were described by mean ± standard deviation (), median, maximum, minimum and quartile, and enumeration data were described by percentage (%). $\bar{x} \pm s$

3. Statistics of data

All the results were analyzed with the use of SPSS, version 23.0. All statistical tests were two-sided, and a *P* value of less than 0.05 was considered to indicate statistical significance. Normally distributed continuous variables were compared among the four groups using analysis of variance (ANOVA), and non-normally distributed variables were compared using the Kruskal-Wallis H test. If normal transformation could not be performed, the rank-sum test was used for comparison. Count data were compared using the chi-square test. Pearson correlation analysis was used for correlation analysis. Ordered logistics regression analysis was used to analyze the influence of general data on the final data. The factorial test focused on the main effects of the two treatments and their interaction. Therefore, repeated measures ANOVA with factorial design was used to analyze the differences in the effects of different treatments and different intervention acupoint areas on the observation area, and Sidak test was used for comparison between groups.

4. Statistical Analysis Plan

Done by professional statisticians. After all data entry and review, the statistician should complete the statistical analysis work in time and issue a written statistical analysis report.

Vii. Final report and publication

After the study, the study report will include a description of the study objectives, the

methods used in the study, and the results and conclusions.

Viii. Quality control

(1) The test SOP should be formulated by the research group.

(2) A special training meeting was held one month before the official start of the clinical trial, and unified training was conducted for all investigators. The implementation plan and standard operating procedures (Sops) were mainly trained to make every clinical researcher familiar with the research process and specific implementation rules, and to ensure the reliability of clinical research conclusions.

(3) All observations in clinical research should be verified and repeatedly confirmed to ensure the reliability and originality of the data, and to ensure that the results and conclusions in clinical research are derived from the original data.

(4) To control the bias of the trial, special personnel should be employed to collect and count the trial data. A professional data management company was commissioned for clinical data management.

(5) The quality inspection of clinical research should be strictly carried out once a month.

Ix. References

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浙江中医药大学附属第三医院医学伦理委员会

伦理审查批件

Approval Letter

批件号 Approval NO.：ZSLL-ZN-2022-026-01 签发日期 Date of issue：2022.12.14

项目名称 Study Title	基于红外热成像技术的委中穴与腰部的关联性研究		
申办方 Sponsor	浙江中医药大学附属第三医院		
主要研究者 Investigator	梁宜	承担专业 Specialty	针灸科
审查类别 Category	初始审查	审查方式 Type of Review	会议审查+快速审查
审查日期 Date of Review	会议审查 2022.12.08 快速审查 2022.12.14		
审查文件清单 Reviewed Items	1. 初始审查申请书 2. 主要研究者专业履历 3. 临床试验方案 中文版本号：1.0 日期： 2022.10.10 4. 知情同意书 中文版本号：2.0 日期： 2022.12.09 5. 病例报告表 中文版本号：1.0 日期： 2022.10.10 6. 招募广告 中文版本号：1.0 日期： 2022.10.10		
审查决定 Decision	委员会对该方案的审查决定为： ■同意 (Approval)		
年度/定期跟踪审查 Continual Review	● 该研究进行过程中将接受伦理委员会的跟踪审查？■是(Yes) □否(No) ● 审查频率为该研究批准之日起每 12 个月一次，首次，请于 2023.12.14 前 1 个月递交研究进展报告。 ● 伦理委员会有根据实际进展情况改变跟踪审查频率的权利。		

浙江中医药大学附属第三医院医学伦理委员会

备注：

1. 请遵循我国相关法律、法规和规章 NMPA《药物临床试验质量管理规范（2020）》、《医疗器械临床试验质量管理规范》（2016）、WMA《赫尔辛基宣言》和 CIOMS《涉及人的健康相关研究国际伦理指南》和国家卫生健康委员会《涉及人的生物医学研究伦理审查办法（2016）》的伦理原则。
2. 请遵循经本伦理委员会批准的临床研究方案、知情同意书、招募材料开展本研究，保护受试者的健康与权利。对研究方案、知情同意书和招募材料等的任何修改，均须得到伦理委员会审查同意后方可实施。
3. 在本院发生的严重不良事件或非预期不良事件应 24 小时内递交本医学伦理委员会，国内其他中心发生的严重不良事件或非预期不良事件需定期汇总后递交本伦理委员会，对于国外发生的非预期不良事件定期汇总后递交伦理委员会，伦理委员会有权对其评估做出新的决定。
4. 自今日起，无论试验开始与否，请在跟踪审查到期前 1 个月提交研究进展报告；若研究正在进行中，请在批件到期前 2 个月，递交研究进展报告，须得到伦理委员会审查同意延长批件有效期后方可继续进行。
5. 研究者和申办方应当向组长单位伦理委员会提交中心研究进展报告汇总；当出现任何可能显著影响试验进行或增加受试者危险的情况时，请申请人及时向伦理委员会提交书面报告。
6. 研究纳入了不符合纳入标准或符合排除标准的受试者，符合中止试验规定而未让受试者退出研究，给予错误治疗或剂量，给予方案禁止的合并用药等没有遵从方案开展研究的情况；或可能对受试者的权益或健康以及研究的科学性造成不良影响等违背 GCP 原则的情况，请研究者和申办者提交违背方案报告。
7. 申请人暂停或提前终止临床研究，请及时提交暂停或终止研究报告。
8. 完成临床研究，请申请人提交结题报告。

主任签字 Chair Signature	
批准日期 Approval Date	2022.12.14
伦理委员会 Stamp	浙江中医药大学附属第三医院医学伦理委员会（盖章）
批件有效期 Period of Validity	此批件的有效期为（2022.12.14-2023.12.13），逾期未实施的，自行废止。
声明 Statement	本伦理委员会的职责、人员组成、操作程序及记录遵循中华人民共和国药品监督管理局颁布的药物临床试验质量管理规范（2020）、医疗器械临床试验质量管理规范（2016）和 ICH-GCP 的伦理审查原则，并遵守中国的相关法律及法规。