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# Effects of Pulsed Low Frequency Magnetic Field Therapy on Pain Intensity in Patients with Musculoskeletal Chronic Low Back Pain: A Randomized Double Blind Placebo Controlled Trial.

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## ABSTRACT

**Introduction:** The aim of the present study is to investigate the effectiveness of pulsed low frequency magnetic field (PLFMF) on the management of chronic low back pain (CLBP).

**Methods and Analysis:** A randomized double blinded controlled clinical trial will be conducted, involving 200 patients with CLBP. Participants will be randomized in a 1:1 ratio to receive either active PLFMF (experimental arm) or sham treatment (control arm) using a permuted-block design which will be stratified according to three subtypes of musculoskeletal CLBP (nociceptive, peripheral neuropathic or central sanitization). Intervention consists of 3 sessions/week for 6 weeks. The primary outcome is the percentage change in Numeric Rating Scale (NRS) pain at week-24 after treatment completion with respect to baseline. Secondary outcomes includes percentage NRS pain during treatment and early after treatment completion, short form 36 quality of life, Roland and Morris Disability Questionnaire; Depression Anxiety Stress Scale 21, Patient Specific Functional Scale, Global perceived effect of condition change, Pittsburgh Sleep Quality Index and Modified Fatigue Impact scale. Measures will be taken at baseline, 3 and 6 weeks during intervention and 6, 12 and 24 weeks after completing the intervention. Adverse events between arms will be evaluated. Data will be analyzed on an intention-to-treat basis.

**Conclusion**: This randomized trial is powered to assess the effectiveness of PLFMF on the management of musculoskeletal CLBP.

**Ethics and dissemination:** The study is funded by Imam Abdulrahman Bin Faisal University (IAU). It has been approved by the IRB of IAU (IRB- 2017-03-129). The study will be conducted at King Fahd Hospital of the University and will be monitored by the Hospital monitoring office for research and research ethics. The trial is scheduled to begin September

2018. Results obtained will be presented in international conferences and will be published in peer-reviewed journals.

**Trial registration number** ACTRN12618000921280, prospectively.

**Key words:** Low back pain, Pulsed low frequency magnetic field, Randomized double blinded controlled clinical trial, Efficacy, Safety

**Strengths and limitations of this study**

- The present study is a well-designed trial to investigate the long-term efficacy and safety of PLFMF on the management of musculoskeletal chronic low back pain.
- Subgroup analysis investigating efficacy of PLFMF on various subtypes of pain based on pain mechanism will be performed. This may help to explain controversial results reported by previous clinical trials.
- Outcome measures include various aspects of low back pain problems (pain intensity as well as disabilities, functional limitations, sleep quality and quality of life).
- All outcome measures used in the present trial are self-report which may potentiate pain and other measured outcome.

## INTRODUCTION

Chronic low back pain (CLBP) is pain or discomfort localized in the lumbosacral region, with or without leg pain (sciatica) that persists for more than 3 months.[1] Eight out of every 10 adults will experience low back pain (LBP) at least once in their life with more than 60% of such cases have a recurrent LBP.[2] The causes of LBP are many, they can range from simple spasm or mechanical causes to more serious causes such as herniated disc and different types of cancer.[3] Symptoms of LBP may vary from one patient to another. In many patients the symptoms may go beyond pain to lead to severe consequences such as sleep disturbances, psychological and social problems which may affect the quality of life .[4] CLBP accounts for about 15% of all cases of LBP, however, it has been reported to be the world-leading source of disability.[5] In addition, CLBP is often associated with socioeconomic burden and psychological distress.[6] For example, the treatment cost for low back pain in the US is estimated to be more than $90 billion per year[7] and $17 billion per year in the UK.[8]

LBP can be classified based on several criteria. It has been classified to acute and chronic based on how long the pain has persisted. It can also be classified into inflammatory and neuropathic based on the underlying mechanism.[9] The main issue is how to differentiate the various subtypes clinically. In many occasions differentiating the various phenotypes clinically is difficult. Smart et al.[10-12] proposed a mechanism based classification to differentiate between different types of musculoskeletal LBP (central sensitization, peripheral neuropathic and nociceptive).

Most of mechanical low back pain respond to rest and various physical modalities. Different conservative and surgical interventions have been used to manage CLBP; however, the optimal therapy is still debatable.[13] Many physical therapy interventions were tried in the management of

CLBP such as soft tissue mobilization and neurodynamic techniques,[14-15] massage therapy,[16] ultrasound, laser therapy and shock wave therapy,[17] exercises,[18] Pilates practice[19] and acupuncture.[20] While some of the rehabilitation interventions were effective on the short term, none of such interventions produced long term effectiveness in the management of CLBP.

Many pharmacological interventions have been used to manage CLBP. For example non-steroid anti-inflammatory drugs and trammel were mildly to moderately effective in reducing pain without much effects on function.[16] Similarly, opioids, benzodiazepines and duloxetine effects on reducing CLBP were small without inducing any improvement in functions.[21] Other drugs were used such as Tricyclic antidepressants, gabapentin, however, their efficacy were not established.[22] Since the CLBP persist for long term, pharmacological interventions are not a suitable solution due to many reasons. Such reasons include toxicity due to long term use, side and adverse effects in addition to problems with tolerance and addiction.[23] Surgical procedures have been used in some cases of CLBP with mixed outcome,[24] however, many patients are reluctant to go through surgery. Add to that the high cost of the surgery to the health care system. Furthermore, the number of what is called "failed back surgery syndrome" are in the rise.[25] Since the conservative approaches currently used to manage CLBP do not seem to be effective on the long term, new approaches are needed to be developed. The new approaches should be safe, noninvasive and cost effective.

Several lines of evidence indicate that pulsed low frequency magnetic field (PLFMF) may be an attractive option for the management of CLBP. Magnetic field blocked the sensory neuron action potential in cultured neurons;[26] however, it enhanced neuronal growth in the presence of growth factor.[27] In rats, magnetic field suppressed the formation of edema.[28] Weintraub et al.[29] showed that magnetic field has a pronounced anti-nociceptive effect. Robertson et al.[30] showed that

PLFMF affected pain and thermal signals in normal volunteers. Selvam et al.[31] reported that PLFMF restored the calcium ATPase activity of the plasma membrane and produced anti-inflammatory effects. PLFMF also inhibited pain processing in a dose dependent manner.[32] Clinically PLFMF has been used for the treatment of different types of pain. Such as planter fasciitis,[33] lumber radicular pain,[34] postoperative pain,[35] peripheral neuropathy[29] and osteoarthritis.[36] Recently we concluded a study which showed that PLFMF was effective in reducing pain, improving sleep and quality of life in patients with carpel tunnel syndrome.[37]

In the case of CLBP few studies were done and produced conflicting results. While Krammer et al.,[13] Oke and Umebese,[38] and Harden et al.[39] reported that PLFMF was not superior to sham treatment in patients with CLBP other studies reported that PLFMF significantly reduced pain intensity in patients with CLBP.[40-42] Most of the six studies which tested the effects of PLFMF on CLBP suffered from methodological problems and flaws. Such problems included failure to perform intention to treat as well as lack of proper blindness of patients and researchers. All these studies failed classify the CLBP into different subgroups since CLBP is heterogeneous. Two of the studies reporting positive findings failed to compare PLFMF with other therapeutic modality.[41-42] All the mentioned studies used small number sample sizes (16 – 40 patients). Some of these studies did not do any follow-up after the conclusion of the interventions or a follow-up for short period.[43] Finally the six studies used different machine producing different magnetic field intensity and frequency and different treatment protocols. Similarly, various studies reported controversial results regarding the effects of PLFMF on level of disability and quality of life in patients with CLBP. Some studies reported that PLFMF improved level of disability and/or quality of life[40-41,44] while other studies reported no effects for PLFMF on disability and/or quality of life.[13,42,45] Two systematic reviews investigated the effects of PLFMF on CLBP. Andrade et al.[43] concluded that PLFMF treatment is superior to placebo treatment. However,

Hug and Roosli[46] concluded that available evidence is not sufficient to recommend the use of PLFMF clinically. Both reviews recommended better controlled randomized studies are needed to clarify the effects of PLFMF on CLBP.

PLFMF is known to be safe, non-invasive, low cost, easy to administer and has no known side effects in the management of patients with CLBP.[46] Improving the condition of patients with CLBP will spare the patient going through several rounds of pharmacological and non-pharmacological treatment as well as invasive procedures like surgery with the ultimate goal to improve the patient quality of life.

## OBJECTIVES

The primary objective of this randomized controlled trial is to evaluate the long-term efficacy and safety of PLFMF on the management of CLBP in increasing the percentage change in Numeric Rating Scale (NRS) pain at week-24 with respect to baseline score. The percentage reduction in Numeric Rating Scale (NRS) pain at week-24 will also be evaluated according to various musculoskeletal CLBP subtypes based on pain mechanism (nociceptive versus peripheral neuropathic versus central sanitization).

The secondary objectives are to evaluate the effects of PLFMF on: 1) pain intensity during treatment and early after treatment completion, 2) level of disability, 3) functional levels, 4) sleep quality, 5) quality of life and 6) fatigue in patients with CLBP. The study will also investigate the long term side effects of PLFMF.

This study will also include subgroups exploratory objectives to clarify the role of PLFMF in the management of patients diagnosed with different subtypes of musculoskeletal CLBP. To the best of our knowledge, this trial is the first randomized clinical trial to explore simultaneously the role

of PLFMF in the management of peripheral neuropathic, nociceptive and central sensitization musculoskeletal LBP patients together.

## METHODS and analysis

Study design This is a two-arm randomized, double blind, placebo controlled clinical trial. The study will be coordinated at the King Fahd Hospital. All participants will be recruited from the Hospital (patients referred to the department, additionally flyers will be distributed inviting people to participate). This study is funded through the Imam Abdulrahman Bin Faisal University project grant (number 2017-308-CAMS). Ethical approval has been obtained from the IRB of the Imam Abdulrahman Bin Faisal University (IRB□ 2017□03-129). This study is prospectively registered with the Australian New Zealand clinical Trials Registry (Registration Number ACTRN12618000921280). Table 1 Trial Registration Data Set. This trial protocol has been prepared according the SPIRIT checklist statement.[47]

Insert Table 1 about here

### Sample Size and power calculation

A total sample size of 200 (100 in each arm) will achieve 90% power to detect a mean difference of percentage reduction in Numerical rating scale (NRS) pain of 10% between the two treated arms at week-24. The mean percentage reduction in NRS pain is assumed to be 15% in the control arm (patient treated with SHAM program) and 25% in patients who receive PLFMF therapy. A 25 standard deviation is considered along with a two-sided significance level (alpha) of 5% using a two-sample equal-variance t-test. The sample size allows for 15 percent of patients

lost to follow-up at week 24.

Mechanism-based classification will be used to classify patients into different phenotypes of musculoskeletal CLBP. This method discriminative validity was established.[10-12] All patients will be analyzed collectively. Subgroup analysis will be performed to assess the effect of PLFMF on subtypes of pain.

**Statistical Analysis**

All randomized patients will be analyzed on the intent-to-treat basis. Safety analyses will be performed for all patients who received at least one treatment session. Data will be coded and entered into SPSS program for analysis. Baseline characteristics will be presented by treatment group. Binary and categorical variables will be summarized by frequencies and percentages. Percentages will be calculated according to the number of patients for whom data are available. Where values are missing, the denominator, which will be less than the number of patients assigned to the treatment group will be reported either in the body or a footnote of the summary table. Continuous variables will be summarized by mean and standard deviation as well as by quartiles.

Treatment effect for the primary and continuous secondary outcomes will be assessed through ANCOVA adjusted for the baseline measurement score. Overall treatment effect over time on all continuous outcomes, repeatedly collected over the course of the study, will be estimated using mixed linear models to take into account the correlation within each individual. The mixed linear model will include random intercept adjusted with the baseline score, time as categorical and the interaction between treatment and time.

Categorical binary efficacy measures will be primarily analyzed using logistic regression. All tests will be two-sided with P-values less than 0.05 will be considered significant.

**Eligibility criteria:**

Subjects will be recruited from King Fahd University Hospital (an 800 bed teaching hospital located in the Eastern Province of the Kingdom of Saudi Arabia).

Subjects will be included in the study if they fulfil the followings:

- Clinical evidence of musculoskeletal CLBP including subtype classification (nociceptive versus peripheral neuropathic versus central sanitization);
- Age 18-60 years old;
- Primary complaint of pain (at least a score of 5 out of 10 on a 0-10 NRS) in the area between the 12th rib and buttock crease, with or without leg pain for 3 months or more;

Patient will be excluded if they have any of the followings:

- Pregnant or lactating
- Significant spinal pathology (e.g. spinal fracture, cauda equina syndrome, spinal infective or inflammatory diseases, , metastatic);
- Spinal surgery within the preceding 6 months;
- Recent organ transplants.
- Heart pace maker.
- Cardiac arrhythmia, tachycardia conditions or large aneurysm.
- Heavy psychosis.
- Epileptic episodes.

Exit criteria:

Participants will be withdrawn from the study if:

- Become pregnant;
- Back pain intensify during the trial to a point which need emergency medical intervention;
- Decided to leave the study voluntarily;
- Added a new medications (was not taken before) which may affect the patients LBP condition.
- Lack compliance.

Patients will be instructed to continue any medication they regularly take before the trial, however, they will be instructed not add any new medications that may affect their back pain during the trial period. All prescription and over the counter medications taken by the participants will be recorded.

**Randomization**

Eligible participants will be randomized in a 1:1 ratio to receive either active PLFMF treatment (experimental arm) or sham treatment (control arm). Randomization list will be centrally generated, in a stratified fashion, using a random permuted block design of size four and six. The stratification factor will be subtypes of musculoskeletal CLBP based on pain mechanism (nociceptive versus peripheral neuropathic versus central sanitization). A researcher who is not part of the study screening, evaluation or treatment will allocate the participants in one of the groups using sealed dense, tamperproof and numbered envelopes, prior to recruitment.

**Tool:**

The BEMER 3000 (BEMER Int. AG) will be pre-programmed to deliver PLFMF (An average of 14 μT). The signal comprises of a series of half-wave-shaped sinusoidal intensity variations. The

signal which starts with low values slowly increases and then decreases but it does not go back to the initial value (i.e. stay above zero). The intensity will gradually get denser with the repetition of the sequence leading to an increase in the ups and downs with repetition. Every second this procedure will be repeated 33.3 times with a reversal of polarity every 2 minutes.[48]

**Blinding**

The trial product will be provided in a blinded manner. All the magnetic coils are covered by a cloth. When switched on the device does not produce any sound or heat to keep patients blinded. Furthermore, to maintain the blinding of the investigator (and designated staff) an identic mattress (size) and same colour cloth will be used for all patients independent of treatment group assignment. Patients and all healthcare providers (therapists and physicians) who care for the participants during the study will be strictly blinded to randomized interventions. Only the treating therapist will know what type of treatment the participant will be given. The assessor and the participants will not have access to such information. The blinding codes will be kept at the monitoring office of research and research ethics till the end of the trial unless an emergency developed which requires unbinding. The treating therapist will be asked not to mention or talk about the treatment groups to others. Upon the completion of the study each participant will be interviewed to be asked about the group which they think they were at.

**Setting**

The trial will be conducted at the department of physical therapy of King Fahd Hospital of the University. King Fahd Hospital of the University is an 800 beds teaching hospital located at the Eastern Province of the Kingdom of Saudi Arabia. All researchers are clinicians at the departments of physical therapy and orthopedics. The trial is scheduled to begin September 2018.

**Procedure**

All screening, interventions and evaluation will be done by qualified musculoskeletal physical therapists who have 5 or more years of clinical experience. Potential participants will be asked to participate in the study, if agreed they will be screened for inclusion and exclusion criteria then they will be asked to sign a consent form. Subjects will be classified to into peripheral neuropathic, nociceptive or central sensitization musculoskeletal LBP according to Smart et al.[10-12] Each participant will be assigned randomly to either the experimental group which will receive PLFMF and the conventional physical therapy program or the control group which will receive sham PLFMF and the conventional physical therapy program. Patients will be asked to lie down on the magnetic mattress for 20 minutes/session, three sessions a week for a total of 18 sessions (6 weeks). In the treatment group, the BEMER mattress will be activated whereas in the control group (placebo), no magnetic field will be generated. The conventional physical therapy program consists of:

- Hot packs (to cover the lower back area) for 20 minutes;
- Back, hamstring and calf muscles stretching (performed from long setting position)
- Lumbar erector spinae muscles self-stretching;
- back muscles strengthening (back extension and bridging);
- Abdominal muscles strengthening (posterior pelvic tilt and sit ups);
- Participants will be asked to hold the above positions for 5 seconds. Each exercise will be done 5 times per session with 1 minute rest between any two repetitions.

Each session will last for 60 minutes as follows:

- 20 minutes for active PLFMF or placebo

- 20 minutes for hot packs
- 20 minutes for exercises.

Treating therapist will monitor adherence to the two intervention sessions using a study calendar.

All patients will be evaluated at baseline, end of the 3rd and the 6th week. To assess for effects persistence, participants will be evaluated at 6 weeks, 12 weeks and 24 weeks after completing the 6-week treatment (Figure 1).

Insert Figure 1 about here

**Outcome Measures**

1. Numerical rating scale (NRS): Pain severity will be measured by the NRS. It is an 11-point numeric scale with one extreme labeled as no pain (0) and the other extreme worst pain imagined (10). It is a valid and reliable scale.[49] The patient will be asked to indicate the level of his/her pain immediately before the session and 5 minutes after the intervention.

The percentage change in pain will be calculated at each post-baseline assessment as:

$$100 \text{ x } \frac{(difference\ between\ baseline\ and\ post{-}pain\ NRS\ scores)}{baseline\ NRS\ score}$$

2. Short Form 36 (SF-36)**:** An Arabic version of the SF-36 will be used to assess the quality of life of all participants. The validity and reliability of the Arabic versions of the SF-36 was established in a sample of Saudis.[50]

3. Disability measurement using the Roland and Morris Disability Questionnaire (RMDQ): is a self-reported, condition-specific questionnaire which consists of 24 questions. It is often used to assess LBP disability. It was translated and adopted into Arabic language.[51]
4. Depression Anxiety Stress Scale 21 (Dass 21): a 21 questions scale which assess the emotional state of depression, anxiety and stress. Each question is assessed in a four points likert scale. The validity and reliability of an Arabic version of the scale has been established.[52]
5. Function measurement will be assessed using Patient Specific Functional Scale (PSFS): it is a valid and reliable measure for physical function in musculoskeletal conditions.[53-54] It measures 3-5 physical activities which are important to the patient and s/he is unable to do without difficulties. Patients rates the difficulty with which they do the function in an 11 points likert scale from 0 (unable to do) to 10 (not at all affected).
6. Global perceived effect (GPE) of condition change: is an one question scale which ask the patient to rate improvement/deterioration numerically from -5= much worse to 5 much better. It is has been recommended as one of the outcomes in clinical trials which study chronic pain.[55] The scale validity and reliability has been established.[56]
7. Pittsburgh Sleep Quality Index (PSQI) is a 19 items questionnaire which assess several aspects of sleep quality (sleep duration, disturbances, quality, efficiency, sleep onset latency, medication, and day-time dysfunction). A global score of sleep quality is the total of the various components of the questionnaire. The higher the score the worse the sleep quality. The questionnaire was translated and validated into Arabic language.[57]
8. Modified Fatigue impact scale (MFIS): is a 21 items questionnaire which was evaluate the fatigue effects on quality of life in patients with chronic diseases. A likert scale from

0 (no effect of fatigue) to 4 (maximum effect of fatigue) is used to score each item of the questionnaire.

**Safety Measures**

PLFMF has no known side effects, however, long term side effects of PLFMF have not been evaluated. If side effects developed or the symptoms of any participants get worse during the study s/he will be given appropriate medical care till the situation is resolved. Such participants will be withdrawn from the trial, if necessary. Any observed side effects will be recorded and reported to the IRB office at Imam Abdulrahman Bin Faisal University.

**Privacy and confidentiality**

Screening, assessment and treatment will be done in a private area at King Fahd Hospital of the University in the department of physical therapy. Data will coded, only one of the researchers will have the key for the codes. All data will be saved in a secured computer protected with a password. Only researchers will have access to data. Upon report writing and professional publication data will be presented collectively, none of the participants' identity will be identified.

**Ethics and dissemination**

The trial was approved by the IRB of the Imam Abdulrahman Bin Faisal University (IRB□ 2017□03-129). Any amendment to the protocol which may impact on the conduct of the study will be approved by the IRB at Imam Abdulrahman Bin Faisal University before implementation. The trial is also registered with the Australian New Zealand Clinical Trial Registry (Registration Number ACTRN 12618000921280). The trial was registered May 31 2018. While the trial being conducted the monitoring office for research and research ethics at

King Fahd Hospital of the University (where the study will be conducted) will monitor the various milestones of the trial. The study will be explained to all participants by one of the researchers. All participants will sign a consent form before the beginning of any procedures of the study.

The results of the present trial will be presented in international conferences and will be published in peer-reviewed journals.

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**Author contributions** Study concept, design and drafting of the manuscript: FAA and SA. Critical revision of the manuscript for important intellectual content: MSA, FA, HK. SL contributed to statistical design and data analysis. All authors critically read and approved the final version of the manuscript.

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**Trial sponsor** Deanship of Research, Imam Abdulrahman Bin Faisal University

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This trial sponsor had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

**Competing interest** None declared.

**Patient consent** Obtained.

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| Data category | Information |
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| Primary registry and trial identifying number | Australian New Zealand Clinical Trial Registry ACTRN 12618000921280) |
| Date of registration in primary registry | 31/05/2018 |
| Secondary identifying numbers | IAU-2017-308-CAMS |
| Source(s) of monetary or material support | King Fahd Hospital of the University |
| Primary sponsor | Imam Abdulrahman Bin Faisal University |
| Secondary sponsor(s) | None |
| Contact for public queries | Fuad A. Abdulla, PhD, PT<br>+966 13 3331308<br>faabdullah@iau.edu.sa |
| Contact for scientific queries | Fuad A. Abdulla, PhD, PT<br>+966 13 3331308<br>faabdullah@iau.edu.sa |
| Public title | Effects of Pulsed Low Frequency Magnetic Field Therapy on Pain Intensity in Patients with Musculoskeletal Chronic Low Back Pain: A Randomized Double Blind Placebo Controlled Trial. |
| Scientific title | Effects of Pulsed Low Frequency Magnetic Field Therapy on Pain Intensity in Patients with Musculoskeletal Chronic Low Back Pain: A Randomized Double Blind Placebo Controlled Trial. |
| Countries of recruitment | Saudi Arabia |
| Health condition(s) or problem(s) studied | Chronic Low Back Pain |
| Intervention(s) | Active comparator: Pulsed low frequency magnetic field (PLFMF, an average of 14 micro tesla for 20 minutes) and the conventional physical therapy program (3 times per week for 6 weeks).<br>Placebo comparator: sham PLFMF (the machine will not be activated, i.e. no magnetic field will be generated, for 20 minutes) and the conventional physical therapy program (3 times per week for 6 weeks).<br>The conventional physical therapy program consists of:<br>• Hot packs for 20 minutes;<br>• Back, hamstring and calf muscles stretching (performed from long setting position)<br>• Lumbar erector spinae muscles self-stretching;<br>• back muscles strengthening (back extension and bridging);<br>• Abdominal muscles strengthening (posterior pelvic tilt and sit ups);<br>Participants will be asked to hold the above positions for 5 seconds. Each exercise will be done 5 times per session with 1 minute rest between any two repetitions. |
| Key inclusion and exclusion criteria | Ages eligible for study: 18 – 60 years<br>Sexes eligible for study: both<br>Accepts healthy volunteers: no<br>Inclusion Criteria:<br>• Clinical evidence of musculoskeletal chronic low back pain including subtype classification (nociceptive versus peripheral neuropathic versus central sanitization);<br>• Age 18-60 years old;<br>• Primary complaint of pain (at least a score of 5 out of 10 on a 0- 10 numerical rating scale) in the area between the 12th rib and buttock crease, with or |

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| | without leg pain for 3 months or more;<br>Exclusion Criteria:<br>• Pregnant or lactating<br>• Significant spinal pathology (e.g. spinal fracture, cauda equina syndrome, spinal infective or inflammatory diseases, , metastatic);<br>• Spinal surgery within the preceding 6 months;<br>• Recent organ transplants.<br>• Heart pace maker.<br>• Cardiac arrhythmia, tachycardia conditions or large aneurysm.<br>• Heavy psychosis.<br>• Epileptic episodes. |
| Study type | Interventional<br>Allocation: randomized<br>Allocation concealment: sealed opaque envelopes<br>Sequence generation: Permuted block randomization<br>Intervention model: parallel assignment<br>Masking: double blind (subject, caregiver, investigator, outcomes assessor)<br>Primary purpose: treatment |
| Date of first enrolment | September 2018 |
| Target sample size | 200 |
| Recruitment status | Will begin Recruiting in July |
| Primary outcome(s) | The percentage change in pain intensity by calculating the percentage change in numerical rating scale (NRS) of pain.<br>The percentage change in pain will be calculated at each post-baseline assessment as:<br>$100 \times \frac{(difference\ between\ baseline\ and\ post{-}pain\ NRS\ scores)}{baseline\ NRS\ score}$<br>All patients will be evaluated at baseline, end of the 3rd and the 6th week from the beginning of intervention. To assess for effects persistence, participants will be also evaluated at 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions. |
| Key secondary outcomes | a. Quality of life assessed using Short Form 36 (SF-36) quality of life questionnaire. Time points: baseline, end of the 3rd and the 6th week from the beginning of intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions.<br>b. Disability assessed by the Roland and Morris Disability Questionnaire. Time points: baseline, end of the 3rd and the 6th week from the beginning of intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions.<br>c. Depression, anxiety and stress assessed by Depression Anxiety Stress Scale 21 questionnaire. Time points: baseline, end of the 3rd and the 6th week from the beginning of intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions.<br>d. Function measurement assessed by Patient Specific Functional Scale. Time points: baseline, end of the 3rd and the 6th week from the beginning of intervention. 6 weeks, 12 weeks and 24 weeks after |

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| | the end of the intervention sessions.<br>e. Change in condition assessed by Global perceived effect of condition change. Time points: baseline, end of the 3rd and the 6th week from the beginning of intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions.<br>f. Quality of sleep assessed by Pittsburgh Sleep Quality Index. Time points: baseline, end of the 3rd and the 6th week from the beginning of intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions.<br>g. Fatigue assessed by Modified Fatigue impact scale. Time points: baseline, end of the 3rd and the 6th week from the beginning of intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions. |

Table 1 Trial Registration Data Set

## Appendix 1

### Consent Form

You are invited to participate in a clinical trial to investigate the long term efficacy and safety of pulsed low frequency magnetic field therapy. The study will be conducted by Prof. Fuad Abdulla, Dr. Saad AlSaadi, Prof. MIR Sadat-Ali, Dr. Fahd AlKhamis, Mr. Hani Alkhawaja and Dr. Serigne Lo (all are affiliated with Imam Abdulrahman Bin Faisal University). The study will be conducted at the department of physical therapy, King Fahd Hospital of the University. Participants in the study will be randomly assigned into two group: group 1 will receive pulsed low frequency magnetic field, hot packs and back exercises while group 2 will receive sham pulsed low frequency magnetic field (i.e. no magnetic field), hot packs and back exercises. Participants are asked to commit one hour three times per week for six weeks for the intervention period then they will be asked to come for evaluation at 6, 12 and 24 weeks after the conclusion of the intervention. At each evaluation time you will asked to rate the pain intensity in your back using an 11 points scale and you will be asked to fill questionnaires to evaluate your quality of life, disability level due to the back pain, psychological status, functional level, effectiveness of intervention received, sleep quality and level of fatigue.

During the intervention period will be asked to lie on a mattress for 20 minutes (which may generate magnetic field or no magnetic field) then hot packs for 20 minutes and back exercises for 20 minutes. You have been selected to participate in this clinical trial because you have chronic low back pain.

Pulsed low frequency magnetic field has no know side effects, however, all participants will be monitored for any type of side effects. If side effects developed or your symptoms get worse during the study you will be given appropriate medical care till the situation is resolved. You may not benefit directly from this research, however, if the pulsed low frequency magnetic field therapy is proven to be effective it will help patients with chronic low back pain. Your participation in this study is on voluntarily basis, you have the right to withdraw from the study at any time without having to provide any reasons for that. Refusal to participate or withdrawal from the study will not affects your rights to the care you are eligible to.

All data collected will be strictly confidential, only researchers involved in this project will have access to your data. All data collected will be coded and analyzed collectively so no participant can be identified when the results are published or presented in conferences.

If you have any questions or concerns please do not hesitate to contact the trial principle investigator Prof. Fuad Abdulla by phone at 13-3331308 or by e-mail faabdullah@iau.edu.sa

I, _____, voluntarily consent to participate in this clinical trial as described above. I have had a chance to ask questions of the researcher, and have had any questions answered to my satisfaction.

_____ _____

Participant Signature Witness Signature

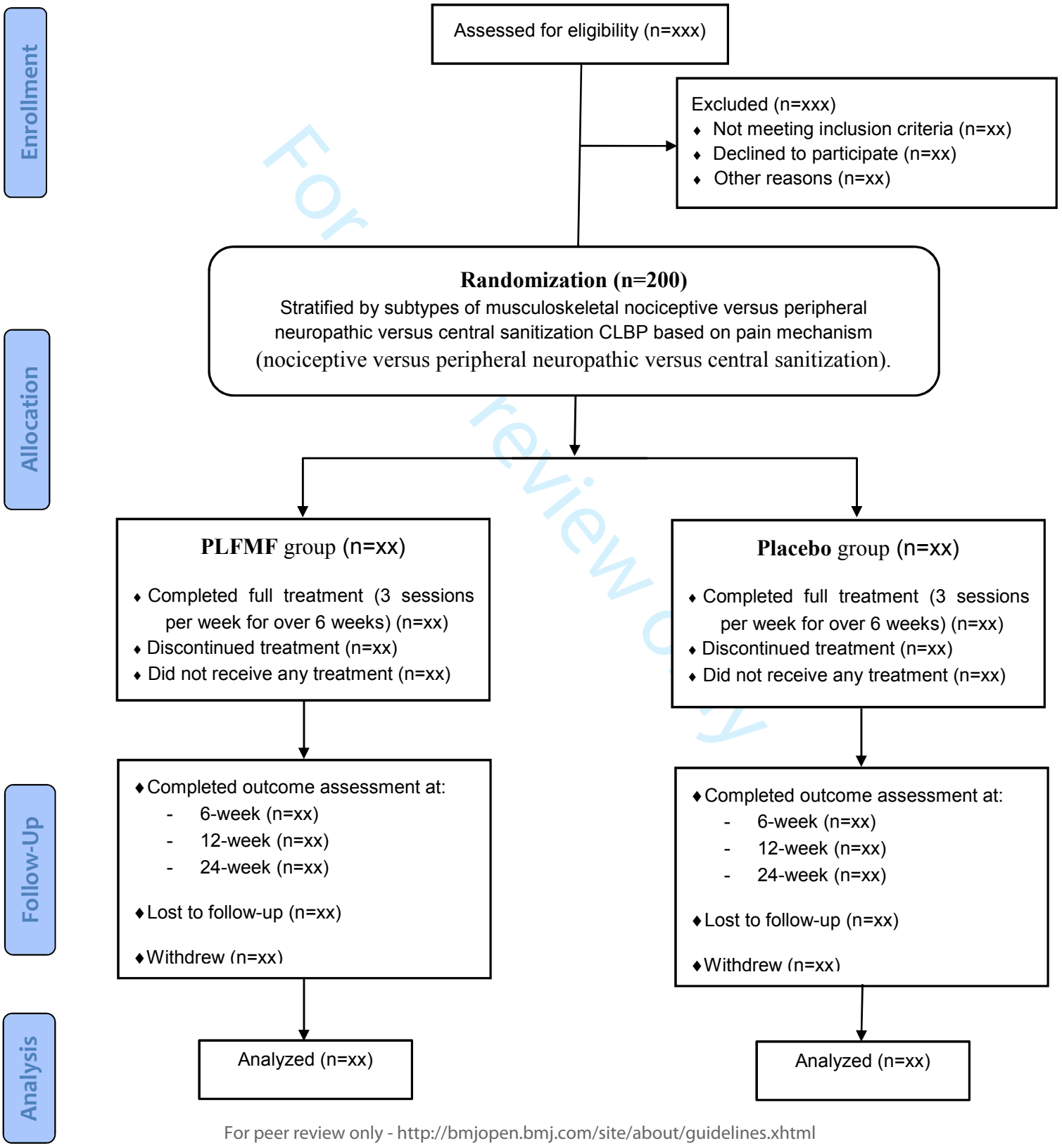
_____

Researcher Signature

_____

Date

**Figure 1**. Flow chart of participation in the 2-arm randomized double blind trial evaluating the efficacy of pulsed low frequency magnetic field therapy (PLFMF) on chronic low back pain (CLBP)



# Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

| | | Reporting Item | Page Number |
|---|---|---|---|
| Title | #1 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym | 1 |
| Trial registration | #2a | Trial identifier and registry name. If not yet registered, name of intended registry | 3 |
| Trial registration: data set | #2b | All items from the World Health Organization Trial Registration Data Set | 23 |
| Protocol version | #3 | Date and version identifier | 17 |
| Funding | #4 | Sources and types of financial, material, and other support | 18 |
| Roles and responsibilities: contributorship | #5a | Names, affiliations, and roles of protocol contributors | 18 |
| Roles and responsibilities: | #5b | Name and contact information for the trial sponsor | 18 |

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| sponsor contact information | | | |
| Roles and responsibilities: sponsor and funder | #5c | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities | 18 |
| Roles and responsibilities: committees | #5d | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) | n/a |
| Background and rationale | #6a | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | 5 |
| Background and rationale: choice of comparators | #6b | Explanation for choice of comparators | 14 |
| Objectives | #7 | Specific objectives or hypotheses | 8 |
| Trial design | #8 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory) | 9 |
| Study setting | #9 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained | 13 |
| Eligibility criteria | #10 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) | 11 |
| Interventions: description | #11a | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered | 13 |

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| Interventions: modifications | #11b | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease) | 11 |
| Interventions: adherance | #11c | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests) | 15 |
| Interventions: concomitant care | #11d | Relevant concomitant care and interventions that are permitted or prohibited during the trial | 12 |
| Outcomes | #12 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended | 15 |
| Participant timeline | #13 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) | 15 |
| Sample size | #14 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations | 9 |
| Recruitment | #15 | Strategies for achieving adequate participant enrolment to reach target sample size | 9 |
| Allocation: sequence generation | #16a | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions | 12 |
| Allocation concealment | #16b | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed | 12 |

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| mechanism | | envelopes), describing any steps to conceal the sequence until interventions are assigned | |
| Allocation: implementation | #16c | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions | 12 |
| Blinding (masking) | #17a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how | 13 |
| Blinding (masking): emergency unblinding | #17b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial | 13 |
| Data collection plan | #18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol | 14 |
| Data collection plan: retention | #18b | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols | 10 |
| Data management | #19 | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol | 10 |
| Statistics: outcomes | #20a | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol | 10 |
| Statistics: additional analyses | #20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) | 10 |
| Statistics: analysis population and missing data | #20c | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) | 10 |

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| Data monitoring: formal committee | #21a | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed | 17 |
| Data monitoring: interim analysis | #21b | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial | 13 |
| Harms | #22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | 17 |
| Auditing | #23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor | 17 |
| Research ethics approval | #24 | Plans for seeking research ethics committee / institutional review board (REC / IRB) approval | 17 |
| Protocol amendments | #25 | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators) | 17 |
| Consent or assent | #26a | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) | 17 |
| Consent or assent: ancillary studies | #26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | n/a |
| Confidentiality | #27 | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial | 17 |
| Declaration of interests | #28 | Financial and other competing interests for principal investigators for the overall trial and each study site | 18 |
| Data access | #29 | Statement of who will have access to the final trial dataset, | 17 |

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| | | and disclosure of contractual agreements that limit such access for investigators | |
| Ancillary and post trial care | #30 | Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation | 17 |
| Dissemination policy: trial results | #31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions | 17 |
| Dissemination policy: authorship | #31b | Authorship eligibility guidelines and any intended use of professional writers | 18 |
| Dissemination policy: reproducible research | #31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code | 18 |
| Informed consent materials | #32 | Model consent form and other related documentation given to participants and authorised surrogates | 27 |
| Biological specimens | #33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable | n/a |

BMJ Open

# Effects of pulsed low frequency magnetic field therapy on pain intensity in patients with musculoskeletal chronic low back pain: study protocol for a randomized-double blind placebo-controlled trial.

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| Journal: | *BMJ Open* |
| Manuscript ID | bmjopen-2018-024650.R1 |
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| Complete List of Authors: | Abdulla, Fuad; Imam Abdulrahman Bin Faisal University, Department of Physical Therapy<br>Alsaadi, Saad; Imam Abdulrahman Bin Faisal University, Department of Physical Therapy<br>Sadat-Ali, MIR; Imam Abdulrahman Bin Faisal University, Department of Orthopedic Surgery<br>Alkhamis, Fahd; Imam Abdulrahman Bin Faisal University, Department of Neurology<br>Alkawaja, Hani; Imam Abdulrahman Bin Faisal University, Department of Physical Therapy<br>Lo, Serigne; Imam Abdulrahman Bin Faisal University, Institute of Research and Medical Consultation; Melanoma Institute Australia |
| Primary Subject Heading: | Rehabilitation medicine |
| Secondary Subject Heading: | Complementary medicine, Evidence based practice |
| Keywords: | Back pain < ORTHOPAEDIC & TRAUMA SURGERY, PAIN MANAGEMENT, REHABILITATION MEDICINE, Clinical trials < THERAPEUTICS, Pulsed low frequency magnetic field, Safety |
| | |

# Effects of pulsed low frequency magnetic field therapy on pain intensity in patients with musculoskeletal chronic low back pain: study protocol for a randomized double-blind placebo-controlled trial

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59 references,

One Table,

One Figure,

Two Appendixes

## ABSTRACT

**Introduction:** The aim of the present study is to investigate the effectiveness of pulsed low frequency magnetic field (PLFMF) on the management of chronic low back pain (CLBP).

**Methods and Analysis:** A randomized double-blinded controlled clinical trial will be conducted, involving 200 patients with CLBP. Participants will be randomized in a 1:1 ratio to receive either active PLFMF (experimental arm) or sham treatment (control arm) using a permuted-block design which will be stratified according to three subtypes of musculoskeletal CLBP (nociceptive, peripheral neuropathic or central sanitization). The intervention consists of 3 sessions/week for 6 weeks. The primary outcome is the percentage change in Numeric Rating Scale (NRS) pain at week-24 after treatment completion with respect to the baseline. Secondary outcomes include percentage NRS pain during treatment and early after treatment completion, short form 36 quality of life, Roland and Morris Disability Questionnaire; Depression Anxiety Stress Scale 21, Patient Specific Functional Scale, Global perceived effect of condition change, Pittsburgh Sleep Quality Index and Modified Fatigue Impact Scale. Measures will be taken at baseline, 3 and 6 weeks during the intervention and 6, 12 and 24 weeks after completing the intervention. Adverse events between arms will be evaluated. Data will be analyzed on an intention-to-treat basis.

**Ethics and dissemination:** The study is funded by Imam Abdulrahman Bin Faisal University (IAU). It has been approved by the IRB of IAU (IRB- 2017-03-129). The study will be conducted at King Fahd Hospital of the University and will be monitored by the Hospital monitoring office for research and research ethics. The trial is scheduled to begin in September

2018. Results obtained will be presented in international conferences and will be published in peer-reviewed journals.

**Trial registration number** ACTRN12618000921280, prospectively.

**Keywords:** Low back pain, Pulsed low frequency magnetic field, Randomized double-blinded controlled clinical trial, Efficacy, Safety

**Strengths and limitations of this study**

- The present study is a well-designed trial to investigate the long-term efficacy and safety of pulsed low frequency magnetic field (PLFMF) on the management of musculoskeletal chronic low back pain.
- Subgroup analysis investigating the efficacy of PLFMF on various subtypes of pain based on pain mechanism will be performed. This may help to explain controversial results reported by previous clinical trials.
- Outcome measures include various aspects of low back pain problems (pain intensity as well as disabilities, functional limitations, sleep quality and quality of life).
- All outcome measures used in the present trial are self-report which may potentiate pain and other measured outcomes.

## INTRODUCTION

Chronic low back pain (CLBP) is pain or discomfort localized in the lumbosacral region, with or without leg pain (sciatica) that persists for more than 3 months.[1] Eight out of every 10 adults will experience low back pain (LBP) at least once in their life with more than 60% of such cases have a recurrent LBP.[2] Evidence suggests that LBP has a lifetime prevalence of 40%, and a mean point prevalence of 20%.[3] The causes of LBP are many, they can range from simple spasm or mechanical causes to more serious causes such as herniated disc and different types of cancer.[4] Symptoms of LBP may vary from one patient to another. In many patients the symptoms may go beyond pain to lead to severe consequences such as sleep disturbances, psychological and social problems which may affect the quality of life.[5] CLBP accounts for about 15% of all cases of LBP, however, it has been reported to be the world-leading source of disability.[6] In addition, CLBP is often associated with the socioeconomic burden and psychological distress.[7] There is no published evidence of LBP cost in Saudi Arabia, the treatment cost for LBP in the US is estimated to be more than $90 billion per year[8] and $17 billion per year in the UK.[9]

LBP can be classified based on several criteria. It has been classified to acute and chronic based on how long the pain has persisted. It can also be classified into inflammatory and neuropathic based on the underlying mechanism.[10] The main issue is how to differentiate the various subtypes clinically. In many occasions differentiating the various phenotypes clinically is difficult. Smart et al.[11-13] proposed a mechanism-based classification to differentiate between different types of musculoskeletal LBP (central sensitization, peripheral neuropathic and nociceptive).

Most of the mechanical low back pain respond to rest and various physical modalities. Different conservative and surgical interventions have been used to manage CLBP; however, optimal therapy is still debatable.[14] Many physical therapy interventions were tried in the management of CLBP such as soft tissue mobilization and neurodynamic techniques,[15 16] massage therapy,[17] ultrasound, laser therapy, and shock wave therapy,[18] exercises,[19] Pilates practice,[20] and acupuncture.[21] While some of the rehabilitation interventions were effective in the short term, none of such interventions produce long term effectiveness in the management of CLBP.[2]

Many pharmacological interventions have been used to manage CLBP. For example, non-steroid anti-inflammatory drugs and trammel were mild to moderately effective in reducing pain without much effects on function.[17] Similarly, opioids, benzodiazepines and duloxetine effects on reducing CLBP were small without inducing any improvement in function.[22] Other drugs were used such as Tricyclic antidepressants, gabapentin, however, their efficacy was not established.[23] Since CLBP persist for long term, pharmacological interventions are not a suitable solution due to many reasons. Such reasons include toxicity due to long term use, side and adverse effects in addition to problems with tolerance and addiction.[24] Surgical procedures have been used in some cases of CLBP with a mixed outcome,[25] however, many patients are reluctant to go through surgery. Add to that the high cost of the surgery to the health care system. Furthermore, the number of what is called “failed back surgery syndrome” is in the rise.[26]

Since the conservative approaches currently used to manage CLBP do not seem to be effective on the long term, new approaches are needed to be developed. The new approaches should be safe, noninvasive and cost-effective.

Several lines of evidence indicate that pulsed low frequency magnetic field (PLFMF) may be an attractive option for the management of CLBP. Magnetic field blocked the sensory neuron action

potential in cultured neurons;[27] however, it enhanced neuronal growth in the presence of growth factor.[28] In rats, magnetic field suppressed the formation of edema.[29] Weintraub et al.[30] showed that magnetic field has a pronounced anti-nociceptive effect. Robertson et al.[31] showed that PLFMF affected pain and thermal signals in normal volunteers. Selvam et al.[32] reported that PLFMF restored the calcium ATPase activity of the plasma membrane and produced anti-inflammatory effects. PLFMF also inhibited pain processing in a dose-dependent manner.[33] Clinically PLFMF has been used for the treatment of different types of pain. Such as plantar fasciitis,[34] lumber radicular pain,[35] postoperative pain,[36] peripheral neuropathy,[30] and osteoarthritis.[37] Recently we concluded a study which showed that PLFMF was effective in reducing pain, improving sleep and quality of life in patients with carpal tunnel syndrome.[38]

In the case of CLBP, few studies were done and produced conflicting results. While Krammer et al.,[14] Oke and Umebese,[39] and Harden et al.[40] reported that PLFMF was not superior to sham treatment in patients with CLBP other studies reported that PLFMF significantly reduced pain intensity in patients with CLBP.[41-43] Most of the studies which tested the effects of PLFMF on CLBP suffered from methodological problems and flaws. Such problems included failure to perform intention to treat as well as lack of proper blindness of patients and researchers. All these studies failed to classify the CLBP into different subgroups since CLBP is heterogeneous. Two of the studies reporting positive findings failed to compare PLFMF with other therapeutic modality.[42 43] All the mentioned studies used small number sample sizes (16 – 40 patients).[44] Some of these studies did not do any follow-up after the conclusion of the interventions or did a follow-up for a short period.[45] Finally, the six studies used different machines producing different magnetic field intensity and frequency and different treatment protocols. Similarly, various studies reported controversial results regarding the effects of PLFMF on the level of disability and quality of life in patients with CLBP. Some studies reported that PLFMF improved

the level of disability and/or quality of life[41 42 46] while other studies reported no effects for PLFMF on disability and/or quality of life.[14 43 47] Two systematic reviews investigated the effects of PLFMF on CLBP. Andrade et al.[45] concluded that PLFMF treatment is superior to placebo treatment. However, Hug and Roosli[48] concluded that available evidence is not sufficient to recommend the use of PLFMF clinically. Both reviews recommended better controlled randomized studies are needed to clarify the effects of PLFMF on CLBP.

PLFMF is known to be safe, non-invasive, low cost, easy to administer and has no known side effects in the management of patients with CLBP.[48] Improving the condition of patients with CLBP will spare the patient going through several rounds of pharmacological and non-pharmacological treatment as well as invasive procedures like surgery with the ultimate goal to improve the patients' quality of life.

## OBJECTIVES

The primary objective of this randomized controlled trial is to evaluate the long-term efficacy and safety of PLFMF on the management of CLBP and on increasing the percentage change in Numeric Rating Scale (NRS) pain at week-24 with respect to baseline score. The percentage reduction in Numeric Rating Scale (NRS) pain at week-24 will also be evaluated according to various musculoskeletal CLBP subtypes based on pain mechanism (nociceptive versus peripheral neuropathic versus central sanitization).[11-13]

The secondary objectives are to evaluate the effects of PLFMF on 1) pain intensity during treatment and early after treatment completion, 2) level of disability, 3) functional levels, 4) sleep quality, 5) quality of life and 6) fatigue in patients with CLBP. The study will also investigate the long term side effects of PLFMF.

This study will also include subgroups exploratory objectives to clarify the role of PLFMF in the management of patients diagnosed with different subtypes of musculoskeletal CLBP. To the best of our knowledge, this trial is the first randomized clinical trial to explore simultaneously the role of PLFMF in the management of peripheral neuropathic, nociceptive and central sensitization musculoskeletal LBP patients together.

## METHODS AND ANALYSIS

**Study design** This is a two-arm randomized, double-blind, placebo-controlled clinical trial. The study will be coordinated at the King Fahd Hospital of the University. All participants will be recruited from the hospital (patients referred to the department, additionally flyers will be distributed inviting people to participate). This study is funded through the Imam Abdulrahman Bin Faisal University (grant number 2017-308-CAMS). Ethical approval has been obtained from the IRB of the Imam Abdulrahman Bin Faisal University (IRB- 2017-03-129). This study is prospectively registered with the Australian New Zealand Clinical Trials Registry (Registration Number ACTRN12618000921280). Table 1 shows Trial Registration Data Set. This trial protocol has been prepared according to the SPIRIT checklist statement (see appendix 1).[49]

Insert Table 1 about here

### Sample size and power calculation

Sample size calculation was based on two sample t-tests. We used R function power.t.test via R version 3.4.1 (https://cran.r-project.org). A total sample size of 200 (100 in each arm) will achieve 90% power to detect a mean difference of percentage reduction in Numerical rating scale (NRS)

pain of 10% between the two treated arms at week-24. The mean percentage reduction in NRS pain is assumed to be 15% in the control arm (patient treated with SHAM program) and 25% in patients who receive PLFMF therapy. A 0.2 standard deviation is considered along with a two-sided significance level (alpha) of 5% using a two-sample equal-variance t-test. The sample size allows for 15 percent of patients lost to follow-up at week 24. A 10% absolute reduction in Numerical rating scale (NRS) pain at week-24 will translate into an expected effect size of 0.5. This means the NRS score of the average person in the active PLFMF arm is 0.5 the standard deviations above the average person who have had sham treatment, and hence exceed the scores of 69% of the control group.

The 38-item clinical criteria checklist developed by Smart et al.[11-13] will be used to classify patients into different phenotypes of musculoskeletal CLBP. This method discriminative validity was established.[11-13] All patients will be analyzed collectively. Subgroup analysis will be performed to assess the effect of PLFMF on subtypes of pain.

**Statistical analysis**

All randomized patients will be analyzed on the intent-to-treat basis. Safety analyses will be performed for all patients who received at least one treatment session. Data will be coded and entered into SPSS program for analysis. Baseline characteristics will be presented by treatment group. Binary and categorical variables will be summarized by frequencies and percentages. Percentages will be calculated according to the number of patients for whom data are available. Where values are missing, the denominator, which will be less than the number of patients assigned to the treatment group, will be reported either in the body or a footnote of the summary table. Continuous variables will be summarized by mean and standard deviation as well as by

quartiles. Before summarizing continuous outcomes, a test of normality will be performed. If the outcome is normally distributed, it will be summarized by mean (standard deviation) in each arm and the difference between arms will be tested using t-test. However, if no evidence of normality, data will be summarized using the median (interquartile range). In such case, the Wilcoxon rank sum test will be used to test the difference between arms.

Treatment effect for the primary and continuous secondary outcomes will be assessed through ANCOVA adjusted for the baseline measurement score. Overall treatment effect over time on all continuous outcomes, repeatedly collected over the course of the study, will be estimated using mixed linear models to take into account the correlation within each individual. The mixed linear model will include random intercept adjusted with the baseline score, time as categorical and the interaction between treatment and time. P-values will not be adjusted for multiplicity. However, the outcomes are clearly categorized by degree of importance (primary, main secondary and other secondary) and a limited number of subgroup analyses are pre-specified.

Categorical binary efficacy measures will be primarily analyzed using logistic regression. All tests will be two-sided with P-values less than 0.05 will be considered significant.

**Eligibility criteria:**

Subjects will be recruited from King Fahd Hospital of the University. Subjects will be included in the study if they fulfill the followings:

- Clinical evidence of musculoskeletal CLBP including subtype classification (nociceptive versus peripheral neuropathic versus central sanitization);
- Age 18-60 years old;

- Primary complaint of pain (at least a score of 5 out of 10 on a 0-10 NRS) in the area between the 12th rib and buttock crease, with or without leg pain for 3 months or more;

Patient will be excluded if they have any of the followings:

- Pregnant or lactating
- Significant spinal pathology (e.g. spinal fracture, cauda equina syndrome, spinal infective or inflammatory diseases, metastatic);
- Spinal surgery within the preceding 6 months;
- Recent organ transplants;
- Heart pacemaker;
- Cardiac arrhythmia, tachycardia conditions or large aneurysm;
- Heavy psychosis;
- Epileptic episodes.

Exit criteria:

Participants will be withdrawn from the study if:

- Become pregnant;
- Back pain intensify during the trial to a point which needs emergency medical intervention;
- Decided to leave the study voluntarily;
- Added new medications (was not taken before) which may affect the patients LBP condition.
- Lack of compliance.

Patients will be instructed to continue any medication they regularly take before the trial, however, they will be instructed not to add any new medications that may affect their back pain during the trial period. All prescription and over the counter medications taken by the participants will be recorded.

**Randomization**

Eligible participants will be randomized in a 1:1 ratio to receive either active PLFMF treatment (experimental arm) or sham treatment (control arm). Randomization list will be centrally generated, in a stratified fashion, using a random permuted block design of size four and six. The stratification factor will be subtypes of musculoskeletal CLBP based on pain mechanism (nociceptive versus peripheral neuropathic versus central sanitization). A researcher who is not part of the study screening, evaluation or treatment will allocate the participants in one of the groups using sealed dense, tamperproof and numbered envelopes, prior to recruitment.

**Tool:**

The BEMER 3000 (BEMER Int. AG) will be pre-programmed to deliver PLFMF (An average of 14 μT) a pulse-frequency of 30 Hz and a pulse duration of 30 ms. The signal comprises of a series of half-wave-shaped sinusoidal intensity variations. The signal which starts with low values slowly increases and then decreases but it does not go back to the initial value (i.e. stay above zero). The intensity will gradually get denser with the repetition of the sequence leading to an increase in the ups and downs with repetition. Every second this procedure will be repeated 33.3 times with a reversal of polarity every 2 minutes.[50]

**Blinding**

The trial product will be provided in a blinded manner. All the magnetic coils are covered by a cloth. When switched on the device does not produce any sound or heat to keep patients blinded. Furthermore, to maintain blinding of the investigator (and designated staff) an identical mattress (size) and same color cloth will be used for all patients independent of treatment group assignment. Patients and all healthcare providers (therapists and physicians) who care for the participants during the study will be strictly blinded to randomized interventions. Only the treating therapist will know what type of treatment the participant will be given. The assessor and the participants will not have access to such information. The blinding codes will be kept at the monitoring office of research and research ethics till the end of the trial unless an emergency developed which requires unblinding. The treating therapist will be asked not to mention or talk about the treatment groups to others. Upon the completion of the study, each participant will be interviewed to be asked about the group which they think they were at.

**Setting**

The trial will be conducted at the department of physical therapy of King Fahd Hospital of the University. King Fahd Hospital of the University is 800 beds teaching hospital located in the Eastern Province of the Kingdom of Saudi Arabia. All researchers are clinicians at the departments of physical therapy and orthopedics. The trial is scheduled to begin in September 2018.

**Procedure**

All screening, interventions, and evaluation will be done by qualified musculoskeletal physical therapists who have 5 or more years of clinical experience. Potential participants will be asked to participate in the study, if agreed they will be screened for inclusion and exclusion criteria then they will be asked to sign a consent form (see appendix 2). Subjects will be classified to peripheral neuropathic, nociceptive or central sensitization musculoskeletal LBP according to criteria established by Smart et al.[11-13] Each participant will be assigned randomly to either the experimental group which will receive PLFMF and the typical physical therapy program used in our department or the control group which will receive sham PLFMF and the typical physical therapy program used in our department. Patients will be asked to lie down on the magnetic mattress for 20 minutes/session, three sessions a week for a total of 18 sessions (6 weeks). In the treatment group, the BEMER mattress will be activated whereas, in the control group (placebo), no magnetic field will be generated. The typical physical therapy program used in our department consists of:

- Hot packs (to cover the lower back area) for 20 minutes;
- Back, hamstring and calf muscles stretching (performed from the long sitting position)
- Lumbar erector spinae muscles self-stretching;
- back muscles strengthening (back extension and bridging);
- Abdominal muscles strengthening (posterior pelvic tilt and sit-ups);
- Participants will be asked to hold the above positions for 5 seconds. Each exercise will be done 5 times per session with 1 minute rest between any two repetitions.

Each session will last for 60 minutes as follows:

- 20 minutes for active PLFMF or placebo
- 20 minutes for hot packs

- 20 minutes for exercises.

Treating therapist will monitor adherence to the intervention sessions using a study calendar.

All patients will be evaluated at baseline, end of the 3rd and the 6th week. To assess for effects persistence, participants will be evaluated at 6 weeks, 12 weeks and 24 weeks after completing the 6-week treatment (Figure 1).

Insert Figure 1 about here

**Outcome Measures**

1. Numerical rating scale (NRS): Pain severity will be measured by the NRS. It is an 11-point numeric scale with one extreme labeled as no pain (0) and the other extreme worst pain imagined (10). It is a valid and reliable scale.[51] The patient will be asked to indicate the level of his/her pain immediately before the session and 5 minutes after the intervention.

The percentage change in pain will be calculated at each post-baseline assessment as:

$$100 \text{ x } \frac{(difference\ between\ baseline\ and\ post - pain\ NRS\ scores)}{baseline\ NRS\ score}$$

2. Short Form 36 (SF-36)**:** An Arabic version of the SF-36 will be used to assess the quality of life of all participants. The validity and reliability of the Arabic versions of the SF-36 was established in a sample of Saudis.[52]
3. Disability measurement using the Roland and Morris Disability Questionnaire (RMDQ): is a self-reported, condition-specific questionnaire which consists of 24 questions. It is often used to assess LBP disability. It was translated and adopted into Arabic language.[53]

4. Depression Anxiety Stress Scale 21 (Dass 21): a 21 questions scale which assesses the emotional state of depression, anxiety, and stress. Each question is assessed in a four point likert scale. The validity and reliability of an Arabic version of the scale has been established.[54]
5. Function measurement will be assessed using Patient Specific Functional Scale (PSFS): it is a valid and reliable measure for physical function in musculoskeletal conditions.[55 56] It measures 3-5 physical activities which are important to the patient and s/he is unable to do without difficulties. Patients rate the difficulty with which they do the function in an 11 points likert scale from 0 (unable to do) to 10 (not at all affected).
6. Global perceived effect (GPE) of condition change: is a one question scale which asks the patient to rate improvement/deterioration numerically from -5= much worse to 5 much better. It is has been recommended as one of the outcomes in clinical trials which study chronic pain.[57] The scale validity and reliability has been established.[58]
7. Pittsburgh Sleep Quality Index (PSQI) is a 19 items questionnaire which assesses several aspects of sleep quality (sleep duration, disturbances, quality, efficiency, sleep onset latency, medication, and daytime dysfunction). A global score of sleep quality is the total of the various components of the questionnaire. The higher the score the worse the sleep quality. The questionnaire was translated and validated into Arabic language.[59]
8. Modified Fatigue impact scale (MFIS): is a 21 items questionnaire which evaluates the fatigue effects on quality of life in patients with chronic diseases. A likert scale from 0 (no effect of fatigue) to 4 (maximum effect of fatigue) is used to score each item of the questionnaire.

**Safety measures**

PLFMF has no known side effects, however, long term side effects of PLFMF have not been evaluated. If side effects developed or the symptoms of any participants get worse during the study or the follow-up period s/he will be given appropriate medical care untill the situation is resolved. Such participants will be withdrawn from the trial, if necessary. Any observed side effects will be recorded and reported to the IRB office at Imam Abdulrahman Bin Faisal University.

**Privacy and confidentiality**

Screening, assessment, and treatment will be done in a private area at King Fahd Hospital of the University in the department of physical therapy. Data will be coded, only one of the researchers will have the key for the codes. All data will be saved in a secured computer protected with a password. Only the researchers will have access to data. Upon report writing and professional publication, data will be presented collectively, none of the participants' identity will be identified.

**Patient and public involvement**

Patients and the public were not involved in the development of this study protocol. However, the obvious lack of satisfactory treatment of chronic low back pain was a major motivator for the study team to develop and conduct this study. The finding of the present study will be disseminated to the participants and the community in general through newsletters and presentations in the community.

**Ethics and dissemination**

The trial was approved by the IRB of Imam Abdulrahman Bin Faisal University (IRB- 2017-03-129). Any amendment to the protocol which may impact the conduct of the study will be approved by the IRB at Imam Abdulrahman Bin Faisal University before implementation. The trial is also registered with the Australian New Zealand Clinical Trial Registry (Registration Number ACTRN 12618000921280). The trial was registered May 31, 2018. While the trial being conducted the monitoring office for research and research ethics at King Fahd Hospital of the University (where the study will be conducted) will monitor the various milestones of the trial. The study will be explained to all participants by one of the researchers. All participants will sign a consent form before the beginning of any procedures of the study.

The results of the present trial will be presented in international conferences and will be published in peer-reviewed journals.

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**Author contributions** Study concept, design and drafting of the manuscript: FAA and SA. Critical revision of the manuscript for important intellectual content: MSA, FA, HK. SL contributed to the statistical design and data analysis. All authors critically read and approved the final version of the manuscript.

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This trial sponsor had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

**Competing interest** None declared.

**Patient consent** Obtained.

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| Data category | Information |
|---|---|
| Primary registry and trial identifying number | Australian New Zealand Clinical Trial Registry ACTRN 12618000921280) |
| Date of registration in primary registry | 31/05/2018 |
| Secondary identifying numbers | IAU-2017-308-CAMS |
| Source(s) of monetary or material support | King Fahd Hospital of the University |
| Primary sponsor | Imam Abdulrahman Bin Faisal University |
| Secondary sponsor(s) | None |
| Contact for public queries | Fuad A. Abdulla, PhD, PT<br>+966 13 3331308<br>faabdullah@iau.edu.sa |
| Contact for scientific queries | Fuad A. Abdulla, PhD, PT<br>+966 13 3331308<br>faabdullah@iau.edu.sa |
| Public title | Effects of Pulsed Low Frequency Magnetic Field Therapy on Pain Intensity in Patients with Musculoskeletal Chronic Low Back Pain: A Randomized Double-Blind Placebo Controlled Trial. |
| Scientific title | Effects of Pulsed Low Frequency Magnetic Field Therapy on Pain Intensity in Patients with Musculoskeletal Chronic Low Back Pain: A Randomized Double-Blind Placebo Controlled Trial. |
| Countries of recruitment | Saudi Arabia |
| Health condition(s) or problem(s) studied | Chronic Low Back Pain |
| Intervention(s) | Active comparator: Pulsed low frequency magnetic field (PLFMF, an average of 14 micro tesla for 20 minutes) and the conventional physical therapy program (3 times per week for 6 weeks).<br>Placebo comparator: sham PLFMF (the machine will not be activated, i.e. no magnetic field will be generated, for 20 minutes) and the conventional physical therapy program (3 times per week for 6 weeks).<br>The conventional physical therapy program consists of:<br>• Hot packs for 20 minutes;<br>• Back, hamstring and calf muscles stretching (performed from the long sitting position)<br>• Lumbar erector spinae muscles self-stretching;<br>• back muscles strengthening (back extension and bridging);<br>• Abdominal muscles strengthening (posterior pelvic tilt and sit-ups);<br>Participants will be asked to hold the above positions for 5 seconds. Each exercise will be done 5 times per session with 1 minute rest between any two repetitions. |
| Key inclusion and exclusion criteria | Ages eligible for study: 18 – 60 years<br>Sexes eligible for study: both<br>Accepts healthy volunteers: no<br>Inclusion Criteria:<br>• Clinical evidence of musculoskeletal chronic low back pain including subtype classification (nociceptive versus peripheral neuropathic versus central sanitization); |

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| | • Age 18-60 years old;<br>• Primary complaint of pain (at least a score of 5 out of 10 on a 0- 10 numerical rating scale) in the area between the 12th rib and buttock crease, with or without leg pain for 3 months or more;<br>Exclusion Criteria:<br>• Pregnant or lactating<br>• Significant spinal pathology (e.g. spinal fracture, cauda equina syndrome, spinal infective or inflammatory diseases, metastatic);<br>• Spinal surgery within the preceding 6 months;<br>• Recent organ transplants.<br>• Heart pacemaker.<br>• Cardiac arrhythmia, tachycardia conditions or large aneurysm.<br>• Heavy psychosis.<br>• Epileptic episodes. |
| Study type | Interventional<br>Allocation: randomized<br>Allocation concealment: sealed opaque envelopes<br>Sequence generation: Permuted block randomization<br>Intervention model: parallel assignment<br>Masking: double-blind (subject, caregiver, investigator, outcomes assessor)<br>Primary purpose: treatment |
| Date of first enrolment | September 2018 |
| Target sample size | 200 |
| Recruitment status | Will begin Recruiting in July |
| Primary outcome(s) | The percentage change in pain intensity by calculating the percentage change in numerical rating scale (NRS) of pain.<br>The percentage change in pain will be calculated at each post-baseline assessment as:<br>$100 \times \frac{(difference\ between\ baseline\ and\ post - pain\ NRS\ scores)}{baseline\ NRS\ score}$<br><br>All patients will be evaluated at baseline, end of the 3rd and the 6th week from the beginning of the intervention. To assess for effects persistence, participants will be also evaluated at 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions. |
| Key secondary outcomes | a. Quality of life assessed using Short Form 36 (SF-36) quality of life questionnaire. Time points: baseline, end of the 3rd and the 6th week from the beginning of the intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions.<br>b. Disability assessed by the Roland and Morris Disability Questionnaire. Time points: baseline, end of the 3rd and the 6th week from the beginning of intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions.<br>c. Depression, anxiety, and stress assessed by Depression Anxiety Stress Scale 21 questionnaire. Time points: baseline, end of the 3rd and the 6th week from the beginning of the intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions. |

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| | d. Function measurement assessed by the Patient Specific Functional Scale. Time points: baseline, end of the 3rd and the 6th week from the beginning of the intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions.<br>e. Change in condition assessed by Global perceived effect of condition change. Time points: baseline, end of the 3rd and the 6th week from the beginning of the intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions.<br>f. Quality of sleep assessed by the Pittsburgh Sleep Quality Index. Time points: baseline, end of the 3rd and the 6th week from the beginning of the intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions.<br>g. Fatigue assessed by Modified Fatigue impact scale. Time points: baseline, end of the 3rd and the 6th week from the beginning of the intervention. 6 weeks, 12 weeks and 24 weeks after the end of the intervention sessions. |

Table 1 Trial Registration Data Set

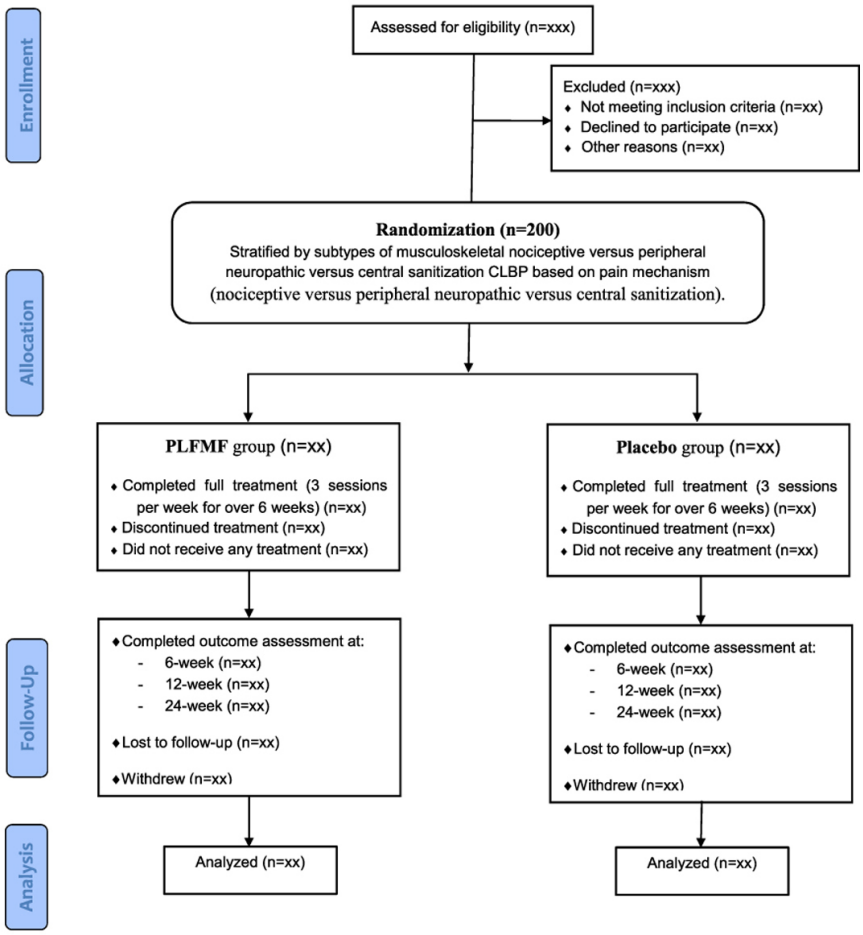


Figure 1. Flow chart of participation in the 2-arm randomized double-blind trial evaluating the efficacy of pulsed low frequency magnetic field therapy (PLFMF) on chronic low back pain (CLBP)

105x105mm (300 x 300 DPI)

# Appendix 1

# Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

## Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRIT reporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

| | | Reporting Item | Page Number |
|---|---|---|---|
| Title | #1 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym | 1 |
| Trial registration | #2a | Trial identifier and registry name. If not yet registered, name of intended registry | 3 |
| Trial registration: data set | #2b | All items from the World Health Organization Trial Registration Data Set | 23 |
| Protocol version | #3 | Date and version identifier | 17 |
| Funding | #4 | Sources and types of financial, material, and other support | 18 |
| Roles and responsibilities: contributorship | #5a | Names, affiliations, and roles of protocol contributors | 18 |

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| Roles and responsibilities: sponsor contact information | #5b | Name and contact information for the trial sponsor | 18 |
| Roles and responsibilities: sponsor and funder | #5c | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities | 18 |
| Roles and responsibilities: committees | #5d | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) | n/a |
| Background and rationale | #6a | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | 5 |
| Background and rationale: choice of comparators | #6b | Explanation for choice of comparators | 14 |
| Objectives | #7 | Specific objectives or hypotheses | 8 |
| Trial design | #8 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory) | 9 |
| Study setting | #9 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained | 13 |
| Eligibility criteria | #10 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) | 11 |

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| Interventions: description | #11a | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered | 13 |
| Interventions: modifications | #11b | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease) | 11 |
| Interventions: adherance | #11c | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests) | 15 |
| Interventions: concomitant care | #11d | Relevant concomitant care and interventions that are permitted or prohibited during the trial | 12 |
| Outcomes | #12 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended | 15 |
| Participant timeline | #13 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) | 15 |
| Sample size | #14 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations | 9 |
| Recruitment | #15 | Strategies for achieving adequate participant enrolment to reach target sample size | 9 |
| Allocation: sequence generation | #16a | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that | 12 |

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| | | is unavailable to those who enrol participants or assign interventions | |
| Allocation concealment mechanism | #16b | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned | 12 |
| Allocation: implementation | #16c | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions | 12 |
| Blinding (masking) | #17a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how | 13 |
| Blinding (masking): emergency unblinding | #17b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial | 13 |
| Data collection plan | #18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol | 14 |
| Data collection plan: retention | #18b | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols | 10 |
| Data management | #19 | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol | 10 |
| Statistics: outcomes | #20a | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol | 10 |

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| Statistics: additional analyses | #20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) | 10 |
| Statistics: analysis population and missing data | #20c | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) | 10 |
| Data monitoring: formal committee | #21a | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed | 17 |
| Data monitoring: interim analysis | #21b | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial | 13 |
| Harms | #22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | 17 |
| Auditing | #23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor | 17 |
| Research ethics approval | #24 | Plans for seeking research ethics committee / institutional review board (REC / IRB) approval | 17 |
| Protocol amendments | #25 | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators) | 17 |
| Consent or assent | #26a | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) | 17 |
| Consent or assent: ancillary studies | #26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | n/a |

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| Confidentiality | #27 | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial | 17 |
| Declaration of interests | #28 | Financial and other competing interests for principal investigators for the overall trial and each study site | 18 |
| Data access | #29 | Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators | 17 |
| Ancillary and post trial care | #30 | Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation | 17 |
| Dissemination policy: trial results | #31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions | 17 |
| Dissemination policy: authorship | #31b | Authorship eligibility guidelines and any intended use of professional writers | 18 |
| Dissemination policy: reproducible research | #31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code | 18 |
| Informed consent materials | #32 | Model consent form and other related documentation given to participants and authorised surrogates | 27 |
| Biological specimens | #33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable | n/a |

## Appendix 2

### Consent Form

You are invited to participate in a clinical trial to investigate the long term efficacy and safety of pulsed low frequency magnetic field therapy. The study will be conducted by Prof. Fuad Abdulla, Dr. Saad AlSaadi, Prof. MIR Sadat-Ali, Dr. Fahd AlKhamis, Mr. Hani Alkhawaja and Dr. Serigne Lo (all are affiliated with Imam Abdulrahman Bin Faisal University). The study will be conducted at the department of physical therapy, King Fahd Hospital of the University. Participants in the study will be randomly assigned into two groups: group 1 will receive pulsed low frequency magnetic field, hot packs and back exercises while group 2 will receive sham pulsed low frequency magnetic field (i.e. no magnetic field), hot packs and back exercises. Participants are asked to commit one hour three times per week for six weeks (the intervention period) then they will be asked to come for evaluation at 6, 12 and 24 weeks after the conclusion of the intervention. At each evaluation time you will be asked to rate the pain intensity in your back using an 11 points scale and you will be asked to fill questionnaires to evaluate your quality of life, disability level due to the back pain, psychological status, functional level, effectiveness of intervention received, sleep quality and level of fatigue.

During the intervention period will be asked to lie on a mattress for 20 minutes (which may generate a magnetic field or no magnetic field) then hot packs for 20 minutes and back exercises for 20 minutes. You have been selected to participate in this clinical trial because you have chronic low back pain.

Pulsed low frequency magnetic field has no known side effects, however, all participants will be monitored for any type of side effects. If side effects develop or your symptoms get worse during the study you will be given appropriate medical care till the situation is resolved. You may not benefit directly from this research, however, if the pulsed low frequency magnetic field therapy is proven to be effective it will help patients with chronic low back pain. Your participation in this study is on a voluntary basis, you have the right to withdraw from the study at any time without having to provide any reasons for that. Refusal to participate or withdrawal from the study will not affect your rights to the care you are eligible to.

All data collected will be strictly confidential, only researchers involved in this project will have access to your data. All data collected will be coded and analyzed collectively so no participant can be identified when the results are published or presented in conferences. The study is funded by deanship of research at Imam Abdulrahman Bin Faisal University.

If you have any questions or concerns please do not hesitate to contact the trial principal investigator Prof. Fuad Abdulla by phone at 13-3331308 or by e-mail faabdullah@iau.edu.sa

I, _____, voluntarily consent to participate in this clinical trial as described above. I have had a chance to ask questions of the researchers, and have had any questions answered to my satisfaction.

_____ _____

Participant Signature Witness Signature

_____

Researcher Signature

_____

Date