PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Ultrasound-guided pulsed radiofrequency versus dry needling for pain management in chronic neck and shoulder myofascial pain patients at a tertiary hospital in China: A randomized controlled trial protocol
AUTHORS	Wang, Jin; Zhang, Yuelun; Cui, Xulei; Shen, Le

VERSION 1 – REVIEW

REVIEWER	Dion Diep University of Toronto Faculty of Medicine
REVIEW RETURNED	08-Feb-2023

GENERAL COMMENTS	Thank you for all your hard work in preparing this protocol of a prospective single-centre RCT comparing between US-guided DN and US-guided PF in MPS. To my knowledge, there is currently no trial comparing these interventions. Given the limitations of comparing these individual interventions to their sham counterparts, a study like this that focuses on effectiveness rather than efficacy is novel and will add to our understanding of MPS treatment. It was a pleasure reviewing your work. Overall, I advise the authors to consider the following: Introduction - The mechanisms for dry needling listed in the third paragraph are hypotheses and should be framed as such. The wording used in the third paragraph where dry needling is introduced currently suggests proven mechanisms of pain alleviation of increasing endplate discharge and reducing acetylcholine stores. Please adjust this sentence and subsequent sentences to ensure that the reader understands that these are just few of the plausible mechanisms. Also please consider using primary sources as your references in this case. - Additional elaboration should be added as to why a comparison between US-guided DN and US-guided PRF is warranted. The introduction only goes as far as introducing both modalities, but does not explain the rationale behind why it is important to compare between both interventions. Is the purpose to demonstrate effectiveness of interventions given that placebo/sham comparisons of each individual intervention is limited? Please elaborate. Methods - Please state in the beginning of the Methods section information regarding ethics approval Eligibility criteria - Simons et al. is appropriately used as a reference when the

BMJ Open: first published as 10.1136/bmjopen-2022-071422 on 24 May 2023. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

	authors state their inclusion criteria for chronic myofascial pain. However, the authors should explicitly state what the diagnostic criteria for chronic myofascial pain is. - Were patients taking general analgesics/pain medications included or excluded? What about patients with psychiatric comorbidities? What about patients who have previously received DN or PF as treatments before? Please elaborate on these potential confounders and explain the rationale for inclusion/exclusion. - Please elaborate on what is meant by a “moderate” pain score on VAS to detect a clinically significant change. Later in the manuscript, it is stated that, there must be a 20mm change to be considered clinically significant (in the Outcomes paragraph). Please clarify the criteria. Preparation and intervention sections - More detail is required to ensure that the intervention is reported comprehensively such that it can be reproduced in future trials. Please consider refering to the TIDieR checklist to ensure adequate reporting of the interventions used. Missing information includes but is not limited to: who the treatment provider is, training of the treatment provider, ultrasound parameters, if the treatments are modified during the trial, etc. Outcomes - Please expand on what the mechanical pain threshold measured by an ergometer is meant to be. Is this pain pressure thresholds? Please ensure the most validated method to measure this. Sample size - Please explain the rationale for the hypothesis that the pain VAS of the PRF group will be 20mm lower than the DN group. Is there any literature to support this? Allocation concealment - Please state the methods used to ensure concealment of allocation Blinding - Efforts seem to be made to ensure patient blinding. However, authors should strongly consider strategies to verify if the blinding technique was effective or not at the end of the study. For instance, patient questionnaires to assess if they can correctly guess their intervention status. Statistical methods - Current statistical methods compare the post-treatment scores between both groups. However, given the very small sample size and anticipated variation of pain scores of participants recruited, it is not unreasonable to anticipate baseline differences between both groups. Is there a plan to account for this covariate? Are there other plans to account for other possible covariates such as concurrent analgesic use, gender, etc.? - I think this study would benefit from a review by a statistician General comments: - Please double check the manuscript to ensure proper grammar. For instance, under the “Follow up” section, “Follow-up will be completed during an outpatient visit by an experienced clinician blinds to group allocation at 0, 1, 3, and 6 months after the entire treatment program ends,” is written. This should be re-written to something such as: “Follow-up will be completed during an

BMJ Open: first published as 10.1136/bmjopen-2022-071422 on 24 May 2023. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

	outpatient visit by an experienced clinician blinded to group allocation at 0, 1, 3, and 6 months after cessation of the treatment program.”

REVIEWER	Fabio Stieven Federal University of Health Sciences of Porto Alegre, Health Science
REVIEW RETURNED	12-Feb-2023

GENERAL COMMENTS	I appreciate the opportunity to review the manuscript. I made some comments to qualify a possible publication of the complete study. I think the manuscript presents a relevant proposal topic for research and clinical practice. However, I have some concerns regarding methodological and statistical aspects and with the predicted intervention model. This trial protocol aims to compare the effects of DN and PRF in neck and shoulder myofascial pain patients. Based on this, I think it would be important to add this information in the title of the manuscript, clearly informing the purpose of the study. I also suggest adding 2-3 sentences in the introduction, focusing on the results of previous clinical trials with both therapies. Specific considerations: 1. I believe that the sample size calculation should be reconsidered. Twenty-two participants are a very small sample size for a trial with 6 six months of follow-up. I think this would make it difficult to interpret the results. 2. This is even more of a concern if we consider that the study intends to include individuals with “neck, shoulder, and upper back region”. I believe this creates an important methodological limitation as the study does not provide any method to balance the distribution of these problems in the respective groups. Page 7, line 21, item 2. The study is addressed to individuals with “myofascial pain”, as stated in the title. However, in the section “Eligible criteria” (page 7, line 21), it is mentioned that “Chronic myofascial pain lasting more than three months at the neck, shoulder, and upper back region (22)”. I suggest informing better in the title of the manuscript. Page 7, line 23, item 3. I suggest that authors clearly write the sentence “Have at least a score of “moderate” on the pain VAS”. I suggest clearly explains the cutoff points to consider what is "moderate". What are the exact parameters or cutoff points for this? Page 8, line 13. Threshold of the pain region measured by an ergometer. Ergometer or algometer?????

BMJ Open: first published as 10.1136/bmjopen-2022-071422 on 24 May 2023. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

	Page 9, line 3-8. The use of dry needling presupposes the clinical identification of myofascial trigger points, through anamnesis and palpation. Using only the ultrasound can predispose to the incorrect identification of the points to be treated, creating a kind of placebo treatment or in places that do not need to be treated. Also, what is the criteria for performed 5 times per pain point and extracted after 30 minutes of indwelling? Why leave the needle for 30 minutes in the region? Why perform 5 moves? What is the rationale for using dry needling in this way? Page 13-34 Considering that the study presents 2 groups and 4 times (0, 1, 3, and 6 months), I would like to suggest another method of statistical analysis, such as the use of the mixed linear model. In addition, considering that the study provides a very small sample size, in the case of sample loss, the use of the t-test or Mann-Whitney U test would further hinder the interpretation of the results. Is any data imputation method foreseen to be used in case of sample loss? I suggest clearly adding the use of intent-to-treat analysis as provided by CONSORT.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Introduction

Q: - The mechanisms for dry needling listed in the third paragraph are hypotheses and should be framed as such. The wording used in the third paragraph where dry needling is introduced currently suggests proven mechanisms of pain alleviation of increasing endplate discharge and reducing acetylcholine stores. Please adjust this sentence and subsequent sentences to ensure that the reader understands that these are just few of the plausible mechanisms. Also please consider using primary sources as your references in this case.

A: The sentences have be rephrased as: “The exact analgesic mechanisms have not been unraveled, but it is hypothesized that DN may increase endplate discharge and local blood flow, reduce spontaneous electrical activities and acetylcholine stores, and change the release of descending inhibitory neurotransmitters as well as the central and peripheral sensitization process.”

Two primary references have been added (page 4, line 12-15).

Q: - Additional elaboration should be added as to why a comparison between US-guided DN and US-guided PRF is warranted. The introduction only goes as far as introducing both modalities, but does

BMJ Open: first published as 10.1136/bmjopen-2022-071422 on 24 May 2023. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

not explain the rationale behind why it is important to compare between both interventions. Is the purpose to demonstrate effectiveness of interventions given that placebo/sham comparisons of each individual intervention is limited? Please elaborate.

A: Yes, we elaborated this point in the revised mansucript “To date, there are currently a lack of high-quality studies on the treatment effects of PRF in myofascial pain patients, and it is also unknown whether PRF can exhibit a superior analgesic effect to DN. Since placebo/sham comparison of each individual intervention provides only limited information, we decided to design a parallel study comparing the two interventions together.”(page 5, line 10-14).

Methods

Q: - Please state in the beginning of the Methods section information regarding ethics approval

A: Ethics approval was added (No. JS-3399) at the beginning of the Methods section (page 6, line 4-5).

Q: Eligibility criteria

- Simons et al. is appropriately used as a reference when the authors state their inclusion criteria for chronic myofascial pain. However, the authors should explicitly state what the diagnostic criteria for chronic myofascial pain is.

A: The Simons and Travell’s criteria has been added to the inclusion criteria:“ taut band palpable, exquisite spot tenderness of a nodule in a taut band, patient’s recognition of current pain complaint by pressure on the tender nodule, painful limit to full stretch range of motion” (page 6, line 13-15)

Q: - Were patients taking general analgesics/pain medications included or excluded? What about patients with psychiatric comorbidities? What about patients who have previously received DN or PF as treatments before? Please elaborate on these potential confounders and explain the rationale for inclusion/exclusion.

BMJ Open: first published as 10.1136/bmjopen-2022-071422 on 24 May 2023. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

A: We added the following points into the exclusion criteria: “current or history of taking moderate to strong analgesics, such as tramadol and morphine; history of receiving DN or PRF treatment; patients with psychiatric disease.” (page 6, line 18-25)

Q:- Please elaborate on what is meant by a “moderate” pain score on VAS to detect a clinically significant change. Later in the manuscript, it is stated that, there must be a 20mm change to be considered clinically significant (in the Outcomes paragraph). Please clarify the criteria.

A: A moderate pain VAS is a VAS ≥ 40mm, we further elaborate this point in the revised manuscript (page 6, line 16).

The 20mm criteria has been deleted, since the study sample size has been re-calculated based on a null hypothesis. We initially used it because a previous study (Pain. 2000;88(3):287-94) suggested that a pain VAS change of 20mm is the minimal clinically important difference (MCID). However, this point will be discussed according to the final study results.

Preparation and intervention sections

Q: More detail is required to ensure that the intervention is reported comprehensively such that it can be reproduced in future trials. Please consider refering to the TIDieR checklist to ensure adequate reporting of the interventions used. Missing information includes but is not limited to: who the treatment provider is, training of the treatment provider, ultrasound parameters, if the treatments are modified during the trial, etc.

A: We further refined the description of the two interventions according to the TIDieR checklist (page 7-9, words in red)

The treatment provider and training: “A certified pain clinician with three years of fellowship training and five years of independent clinical practice experience will provide treatment for all participants with assistance from a pain nurse with more than ten years nursing experience.” (page 7, line 19-21)

BMJ Open: first published as 10.1136/bmjopen-2022-071422 on 24 May 2023. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

The ultrasound parameters: “Both interventions will be performed under real-time ultrasound guidance (Sonosite X-port, USA) with the transducer covered by sterilized protective bags. A linear transducer will be placed on the marked pain region to identify the musculoskeletal structures, including the superficial and deep muscle layers, as well as the fascia. The ultrasound parameters will be set as: linear transducer 4-13Hz, MSK general mode, target depth 3-5 cm, medium brightness. (page 8, line 4-7)”

Treatment modification: “Protocol modifications will require a formal amendment to the protocol with agreement from the project management committee (WJ, ZYL, CXL) and updates in the trial registry (Clinicaltrials.gov). Then, a research member will inform the participants. Participants have the right to withdraw from the study at any time. The researchers can also discontinue treatment for a participant’s best interest (eg. severe adverse events). All changes in the participant’s intervention will be recorded in detail in the case report form.” (page 14, line 3-7)

Outcomes

Q:- Please expand on what the mechanical pain threshold measured by an ergometer is meant to be. Is this pain pressure thresholds? Please ensure the most validated method to measure this.

A: It is the pressure pain threshold measured by an algometer.We added the measurement detail in the revised manuscript:“ The pressure pain threshold will be measured at the center of the marked pain region using an algometer with a probe area of 1 cm^2. The algometer will be applied perpendicular to the tissue at a constant rate of approximately 30kPa/s. A 30-second resting period will be allowed between each measure to avoid temporal summation and the average of three trials will be calculated and recorded as the final results.” (page 7, line 23-26)

Sample size

Q: - Please explain the rationale for the hypothesis that the pain VAS of the PRF group will be 20mm lower than the DN group. Is there any literature to support this?

A: The sample size has been re-calculated based on a null hypothesis, hence, there is no need for the 20mm threshold. (We initially used it because previous study (Pain. 2000;88(3):287-94)

BMJ Open: first published as 10.1136/bmjopen-2022-071422 on 24 May 2023. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

suggested that a pain VAS change of 20mm is the minimally clinical importantce difference - MCID). Whether the between-group differences have clinical significance will be discussed according to final study results. (page 10, line 4-8)

Allocation concealment

Q: - Please state the methods used to ensure concealment of allocation

A: According to a pregenerated random sequence, each enrolled patient will be given a sealed opaque envelope based on the order of enrollment. After the patient has been sterilized, a pain nurse will open the sealed envelope and assign the patient to the corresponding group according to the random number in the envelope, and an experienced clinician will perform the corresponding treatment on the patient. (Page 11, line 7-11)

Blinding

Q: - Efforts seem to be made to ensure patient blinding. However, authors should strongly consider strategies to verify if the blinding technique was effective or not at the end of the study. For instance, patient questionnaires to assess if they can correctly guess their intervention status.

A: The Adequacy of blinding will be tested after completion of the treatment by asking the participants to guess whether they received DN or PRF. The questionnaire will have seven choices: certainly DN, certainly PRF, probably DN, probably PRF, possibly DN, possibly PRF, do not know. Participants who select “certainly”, “probably”, “possibly” and are correct about the answer are considered correct. (page 11, line 19-24)

Statistical methods

Q: - Current statistical methods compare the post-treatment scores between both groups. However, given the very small sample size and anticipated variation of pain scores of participants recruited, it is not unreasonable to anticipate baseline differences between both groups. Is there a plan to account for this covariate? Are there other plans to account for other possible covariates such as concurrent

BMJ Open: first published as 10.1136/bmjopen-2022-071422 on 24 May 2023. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

analgesic use, gender, etc.?

- I think this study would benefit from a review by a statistician

A: We referred to a statistician and take his advice to enlarge the sample size (N1=N2=54) based on a null hypothesis. Whether the between group differences in pain scores can achieve clinical significance will be discussed based on final study results. (page 10, line 4-8).

General comments:

Q: - Please double check the manuscript to ensure proper grammar. For instance, under the “Follow up” section, “Follow-up will be completed during an outpatient visit by an experienced clinician blinds to group allocation at 0, 1, 3, and 6 months after the entire treatment program ends,” is written. This should be re-written to something such as: “Follow-up will be completed during an outpatient visit by an experienced clinician blinded to group allocation at 0, 1, 3, and 6 months after cessation of the treatment program.”

A: This sentence has been revised, and we further revised the manuscript using AJE service.

Reviewer: 2

Q: - This trial protocol aims to compare the effects of DN and PRF in neck and shoulder myofascial pain patients. Based on this, I think it would be important to add this information in the title of the manuscript, clearly informing the purpose of the study.

A: The title has been changed into “Ultrasound-guided pulsed radiofrequency versus dry needling for pain management in chronic neck and shoulder myofascial pain patients: A randomized controlled trial protocol” (page 1, line 1-2).

Q: - I also suggest adding 2-3 sentences in the introduction, focusing on the results of previous clinical trials with both therapies.

A: We added it. Page 4, line 16-17, 19-21. Page 5, line 6-8.

BMJ Open: first published as 10.1136/bmjopen-2022-071422 on 24 May 2023. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Specific considerations:

Q: 1. I believe that the sample size calculation should be reconsidered.

Twenty-two participants are a very small sample size for a trial with 6 six months of follow-up. I think this would make it difficult to interpret the results.

2. This is even more of a concern if we consider that the study intends to include individuals with "neck, shoulder, and upper back region". I believe this creates an important methodological limitation as the study does not provide any method to balance the distribution of these problems in the respective groups.

A: We referred to a statistician and take his advice to enlarge the sample size (N1=N2=54) based on a null hypothesis. Page 10, line 4-8.

Q: - Page 7, line 21, item 2.

The study is addressed to individuals with "myofascial pain", as stated in the title. However, in the section "Eligible criteria" (page 7, line 21), it is mentioned that "Chronic myofascial pain lasting more than three months at the neck, shoulder, and upper back region (22)". I suggest informing better in the title of the manuscript.

A: The title has been changed into "Ultrasound-guided pulsed radiofrequency versus dry needling for pain management in chronic neck and shoulder myofascial pain patients: A randomized controlled trial protocol" (page 1, line 1-2).

Q: - Page 7, line 23, item 3.

I suggest that authors clearly write the sentence "Have at least a score of "moderate" on the pain VAS". I suggest clearly explains the cutoff points to consider what is "moderate". What are the exact parameters or cutoff points for this?

A: A moderate pain VAS is a VAS ≥ 40mm, we further elaborate this point in the revised manuscript (page 6, line 16).

Q:- Page 8, line 13.

Threshold of the pain region measured by an ergometer. Ergometer or algometer?????

BMJ Open: first published as 10.1136/bmjopen-2022-071422 on 24 May 2023. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

A: It is algometer. We apologize for the mistake since we are not native speakers. We looked up the dictionary and revised the word in the manuscript.

Q:- Page 9, line 3-8.

The use of dry needling presupposes the clinical identification of myofascial trigger points, through anamnesis and palpation. Using only the ultrasound can predispose to the incorrect identification of the points to be treated, creating a kind of placebo treatment or in places that do not need to be treated.

Also, what is the criteria for performed 5 times per pain point and extracted after 30 minutes of indwelling? Why leave the needle for 30 minutes in the region? Why perform 5 moves? What is the rationale for using dry needling in this way?

A: Both groups will use the palpation method to identify the trigger points and mark it with "×------×" before sterilization. After sterilization and draping, a linear transducer will be put on the marked pain region to identify muscle structures and guide the needle puncture process. (page 7, line 22-23, page 8, line 3-5)

There are currently lacking a consensus on how many times per needling should be done. The reported needling times varied from 3 to 20 times (PMID: 28735825), and indwelling duration varied from 3 to 30 minutes. It is suggested that a 30 minutes indwelling time may be beneficial to patients (PMID:33992269). After reconsideration, we revised the dry needling parameters as: "rapid insertion of the needle in and out of the pain point will be performed in a way similar to Hong's fast-in and fast-out technique. Based on previous study experiences, dry needling will be performed either until local twitch responses are no longer elicited or 8 to 10 times per pain point, and indwelled for 30 minutes." (page 8, line 22-26)

Q: Page 13-34

Considering that the study presents 2 groups and 4 times (0, 1, 3, and 6 months), I would like to suggest another method of statistical analysis, such as the use of the mixed linear model.

In addition, considering that the study provides a very small sample size, in the case of sample loss, the use of the t-test or Mann-Whitney U test would further hinder the interpretation of the results.

BMJ Open: first published as 10.1136/bmjopen-2022-071422 on 24 May 2023. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Is any data imputation method foreseen to be used in case of sample loss?

I suggest clearly adding the use of intent-to-treat analysis as provided by CONSORT.

A: We referred to a statistician and take his advice to enlarge the sample size (N1=N2=54) based on a null hypothesis.

Based on previous studies and our clinical experiences, the postoperative six-month pain VAS will have a highly skewed distribution, hence, the primary outcome, the postoperative six-month pain VAS, will be analyzed using the Mann-Whitney U test.

Secondary outcomes including the pain, psychological, sleep and life quality scale score at different postoperative time points will be analyzed using the mixed-effects linear model.

The last observation carried forward method will be used for data imputation, and the statistical analysis will follow the intention-to-treat principle.

Detailed statistical methods are described in the revised manuscript. (Page 12, line 13-26)

BMJ Open: first published as 10.1136/bmjopen-2022-071422 on 24 May 2023. Downloaded from http://bmjopen.bmj.com/ on June 13, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.