Author's response to reviews

Title: The effect of continuous ultrasound on chronic non-specific low back pain: A single blind sham-controlled randomized trial

Authors:

Safoora Ebadi (s_ebadi@razi.tums.ac.ir)
Noureddin Nakhostin Ansari (nakhostin@sina.tums.ac.ir)
Soofia Naghdi (naghdi@sina.tums.ac.ir)
Shohre Jalaei (jalaeish@tums.ac.ir)
Mirmostafa Sadat (sadat1335@gmail.com)
Hosein Bagheri (hbagheri@tums.ac.ir)
Maurits W vanTulder (maurits.van.tulder@falw.vu.nl)
Nicholas Henschke (nhenschke@georgeinstitute.org.au)
Ehsan Fallah (fallah_e@razi.tums.ac.ir)

Version: 3 Date: 29 May 2012

Author's response to reviews: see over
Dear Editor,

We are pleased to resubmit the revised version of MS: 1444387473641758 “The effect of continuous ultrasound on chronic non-specific low back pain: A single blind sham-controlled randomized trial.” We appreciated the constructive and helpful comments of the reviewers and have addressed each of their concerns as outlined below.

The most substantial revision was the change in the analysis method and the subsequent change of discussion and conclusion parts. In addition, the manuscript has been over read by a native speaker.

Yours sincerely,
Safoora Ebadi

Reviewer: Tim Watson

Major Compulsory Revisions

1) You make the claim in the abstract and elsewhere in the text (intro and discussion) that ultrasound is commonly applied for CLBP. I am not sure that this is true, and you provide no reference material to support your claim and thus to justify your investigation.

Response: In the abstract the sentence “One of the most widely used modalities in the field of physiotherapy for treating CLBP is therapeutic ultrasound” is changed to “One of the most widely used modalities in the field of physiotherapy is therapeutic ultrasound”

2) If you have carried out statistical analyses, it is normal to include the actual p values rather than < or > then 0.05.

Response: actual p values are included according to the reviewer’s comment

3) In your Ultrasound application section you have a reference to Robertson with no reference number - needs to be corrected

The concept that 1MHz ultrasound is used to target chronic conditions is not
consistent with the literature that you have cited elsewhere in this paper. You have not made a specific reference to it - it needs some kind of justification. I appreciate that you can not change what you did, but it needs to be justified none the less

Response:

Thank you for your point. Actually by Robertson we meant the chapter regarding ultrasound in the book “Electrotherapy Explained” which had not been referenced by mistake.

We would like to draw your attention to the following excerpts from Electrotherapy Explained (Robertson, 3rd edition):

- Mild heating in the chronic phase of injury is known to reduce pain and muscle spasm and to promote healing process (Robertson 267).
- Ultrasound frequency of 1 MHz is preferable when treating large soft tissue volumes (263).
- 1 MHz ultrasound is preferable for deeper tissues (p263).
- More chronic lesions are treated with continuous ultrasound (p285).
- Intensities between 0.8 to 3 W/cm² are suggested for chronic lesions [9,21,22].

From above mentioned points and using other electrotherapy references like Belanger2010, Cameron2003 and according to the writer’s previous work 1.5 W/cm² was chosen.

The sentence “We applied ultrasound using Enraf Nonius Sonoplus 434 (coupling gel: Sono Gel, Germany) operating at a frequency of 1 MHz (targeting chronic conditions) and an intensity of 1.5 W/cm² (Robertson).” Was changed to: “Mild heating in the chronic phase of injury is known to reduce pain and muscle spasm and to promote healing process. More chronic lesions are treated with continuous US. Ultrasound frequency of 1 MHz is preferable when treating large and deep soft tissue volumes. Intensities between 0.8 to 3 W/cm² are suggested for chronic lesions [9,21,22]. Therefore, we chose continuous mode with a frequency of 1 MHz and an intensity of 1.5 W/cm² due to the chronocity of the condition, the deep position of lower back musculature and the need to deliver energy to an almost large area.
Ultrasound was applied using Enraf Nonius Sonoplus 434, ENRAF, Netherland (coupling gel: Sono Gel, Germany)

4) The concept that the patient was blinded to the group allocation (verum or placebo) is potentially flawed in that at the dose you have applied, a thermal effect would be expected. If the patient did/did not feel heat, this would have influenced their perception of the therapy.

Response:

We appreciate Dr. Watson's concern greatly and would like to draw your attention to the points below.

“According to Robertson (p276) “it is relatively easy to arrange a double blind trial (for ultrasound) as the patient is unaware of any sensation at most therapeutic intensities.”

The paragraph below was added to the method to elaborate on the placebo ultrasound application.

“Patients in the intervention group received real continuous US. Placebo US was delivered according to Hashish 1988[24]. The therapist moved the applicator at the same rate and pressure as for the real US group. The machine and the light-emitting diode which signaled that its power was connected were in view of the subject, but the dials which indicated the US were out of sight. At the beginning of treatment with US, the patient is not aware of what she/he should expect and since even with real US the patient is unaware of any sensation at most therapeutic intensities [21], patients were told in both groups that they may feel some heat and if its annoying tell the therapist in order to safeguard patients in the real US group from overheating.”
5) You say in your previous paper (ref 14) that you planned to evaluate the patient awareness of group allocation, but in fact did not carry this out. This needs to be addressed in this report.

Response:

Thank you for mentioning this point.
A subheading of Limitation was added to the manuscript addressing the limitations of the study.

6) Outcome measures section

The pain measured using a VAS scale is a common method, but you make no indication whether you were assessing the pain at that moment in time, averaged over the last day, or since the last treatment session or . . . whatever was used. This is known to make a difference to the magnitude and the reliability of the VAS as an outcome measure and needs to be clarified.

Response:

The sentence “Pain measured on a visual analogue scale (VAS).” was changed to “Pain averaged during last week measured on a visual analogue scale (VAS).”

7) Data Analysis

The statistical analysis needs to have a stronger justification - particularly why you did not use a repeated measures ANOVA with post hoc analysis.

Response:

This very helpful and constructive comment of Dr. Watson was explicitly addressed in the method and the statistical analysis was changed to repeated measure ANOVA and consequently discussion was written accordingly.

8) Results paragraph 2: you say that you 'adjusted' for endurance time - but make no statement with regards what this adjustment entailed which should be included.

Response:
The method of investigating the possible effect of endurance time at baseline on the results is added to the result section.

9) Discussion

Your comparison with previous research in this field appears to be inconsistent. At times you say that your results were generally in agreement with paper XX and later you say you were largely different from paper YY, but this appears to be a rather subjective decision.

Response:

Discussion has been largely revised and we have tried to restructure the sentences regarding comparisons to make it more clear.

10) You say that ultrasound effects were no different between the real and sham groups and therefore the effect was placebo based. It could be that ultrasound has no effect in this clinical condition and therefore the improvements were attributable to the exercise alone - the ultrasound made no contribution to the change over time. This is a distinct possibility and should be mentioned. You could only attribute the effects to a placebo response if you had a third group who received no ultrasound (real or sham) and then identified that the real and sham ultrasound group changes were no different from each other, but both were different to the control

Response:

The results of the repeated measure ANOVA showed more improvement of FRI and endurance time as well as lumbar ROM in the real US group. The discussion is changed accordingly and the very useful point of the reviewer has been addressed.
11) Unless ultrasound has a primary effect on the pain experience, it was unlikely to ever have an effect on gross movement (flexion/extension) as it does not have this capability. It can result in changes collagen extensibility and flexibility range, but not in the lumbar spine and not at these doses. There is a 'stretching window' immediately following high dose ultrasound, and if stretching exercise is undertaken in this (short) period, there have been demonstrable chances (previously published work) but this is not the approach that you adopted, and hence it is difficult to imagine how ultrasound could be expected to influence gross spinal mobility.

Similarly ultrasound does not have the capacity to influence muscle endurance, though exercise does. Demonstrating no difference in endurance capacity between groups is therefore not at all surprising. The fact that your exercise programme, common to both groups, also failed to demonstrate any difference (pre-post) is a different issue. Your previous paper (ref 14) indicated that you would use stretching followed by strengthening exercises. You make the same statements in this paper. If that was the intention, then one would question the justification for recording an endurance outcome when the exercise programme appears not to have been designed to influence endurance capacity. This requires some further justification and rationalisation.

Response:

As mentioned in the previous comment the results and discussion parts have been changed fundamentally.

12) Agree that the therapist was not blinded, but one remain unconvinced that the patient was blinded based on the thermal issues identified previously. This needs to be considered

Response:

Delivering placebo ultrasound is previously mentioned in Response to comment 4.
13) You mention that it was 'impossible' to check for compliance with the exercise program. Whilst it is problematic, it is not impossible, and some kind of diary compliance monitoring has been reasonably widely used in other studies. Whilst it is too late for this study, it could reasonably be included in your limitations section.

Response:

Totally correct. The point is mentioned in the limitation section.

13) Given that ultrasound would not be expected to influence spinal mobility nor endurance, I am not sure that your conclusion is justified. Your work does show that the addition of ultrasound to an exercise programme did not make any difference to the outcome on your primary outcomes, and also that the exercise programme as employed in this study did not make any difference to mobility nor endurance etc.

Response:

New analysis showed that ultrasound group had greater improvement regarding function, ROM and endurance time. Discussion and conclusion have been changed accordingly.

Reviewer: Gráinne Kelly

Minor Essential Revisions:

This manuscript reports on a study investigating 'the effect of continuous ultrasound on chronic non-specific low back pain'. The authors have clearly, and adequately addressed the study aims and need for such research. Overall the manuscript is clear, logical and well thought out. Some aspects of the methodology require more detail and clarification. The discussion lacks some depth of thought in relating previous research to the current findings.

Response:

Thank you for your positive point of view. More detail is included in the required parts according to Dr. Kelly’s comments.
General comments:

The manuscript would benefit enormously from proof-reading as there are quite a considerable number of punctuation and character spacing errors throughout, with too many errors to comment on here e.g. are spacing between words and punctuation marks, brackets, and can spacing between separate words. Also consideration should be given to the ‘tense’ in which each section of the manuscript is written, in general past-tense for abstract, methods, results, discussion.

Response:

Punctuation and character spacing errors have been checked thoroughly and a native speaker did a final language check.

1) Abstract:

Results section (final sentence): spelling of lumbar not lumber, also please check throughout manuscript.

Conclusion: The authors conclude that ‘larger trials are needed to confirm the results’, both here and in the discussion section of the manuscript. A revision of this statement is perhaps needed, as it raises the question ‘would differences between groups be seen, even with larger number, and also based on the authors pre study powering?’

Response:

Abstract is changed according to the new analysis and the reviewer’s points have been addressed.

2) Introduction:

Second paragraph commencing ‘specific back pain’ – could the authors remove the words ‘no more than’, to improve sentence structure. Also no reference is included for this statement, could the authors address this.
Response:
“no more than” is deleted.
The reference has come after the second sentence (the one beginning with “for the majority”).

3) Third paragraph commencing ‘non-pharmacological’ – could the authors include a reference(s) for this sentence and the subsequent sentence commencing ‘therapeutic ultrasound’.

Response:

4) Within the same paragraph the authors state that ‘none of the international guidelines have recommended ultrasound for the treatment of non-specific LBP’, could they please detail why this is the case i.e. lack of evidence, and therefore why are they investigating it’s use

Response:
Lack of evidence of effect is not equal to evidence of lack of effect. The lack of evidence, meaning that there are no RCTs (high quality) published, was the main reason for investigating it.

The explanation above is included in the last section of the introduction and the sentence ‘none of the international guidelines have recommended ultrasound for the treatment of non-specific LBP’ is changed.

5) Fourth paragraph, sentence commencing ‘this increased temperature’ – could the authors change the sentence structure to read ‘this increased temperature, named thermal effects, is thought to cause changes in nerve conduction velocity, .....’.
Response:
The sentence is changed to “This increased temperature, named thermal effects, is thought to cause changes in nerve conduction velocity, increase in enzymatic activity, changes in contractile activity of skeletal muscles, increase in collagen tissue extensibility, increase in local blood flow, increase in pain threshold, and reducing muscle spasm”

6) Fifth paragraph – the authors introduce the concept of continuous ultrasound, this section may benefit from a brief description of continuous and pulsed ultrasound, their physiological mechanisms, and why the authors chose to focus on continuous ultrasound

Response:
This sentence is added to the beginning of 5th paragraph “Ultrasound is delivered in two modes. Continuous mode in which the delivery of ultrasound is non-stop throughout the treatment period. Pulsed ultrasound which is delivery of ultrasound during only a portion of the treatment period with on-off phases”

7) Methods: Please write in past-tense throughout.

Response:
The tense is changed.

8) Study design section

First paragraph - include the full written phase for TUMS on initial introduction and then its abbreviation

Response:
The full phrase is added.

9) Second paragraph - restructure introductory sentence to remove personal terminology i.e. ‘We’, e.g. ‘Inclusion criteria for participation in this study was as follows: patients with NSCLBP, aged between 18 and 60, .....’

Response:
The structure is changed accordingly.
10) Intervention section
Second paragraph under ultrasound application – again restructure the sentence commencing with ‘We’ e.g. ‘Ultrasound was applied using Enraf....’.
Second paragraph under ultrasound application - the manufacturer name and country of the Enraf Nonius Sonoplus 434 should be included.
Second paragraph under ultrasound application – reference of Robertson should be numbered and not named. Also a reason should be given as to why these parameters were chosen.
Response:
Changes are made according to reviewer’s comments.

11) First paragraph under exercise therapy – more information is needed on the type of exercise performed, and the rationale for including exercise as a treatment/management strategy
Response:
More information is included in the manuscript under exercise:
“

The results of the 2011 Cochrane review showed that in chronic low-back pain, there is strong evidence that exercise is at least as effective as other conservative treatments. Meta-analysis found functional and pain outcomes significantly improved in groups receiving exercises relative to other comparisons[...]. It has been shown that stretching and muscle strengthening exercises were the best types of exercises for improving pain and function, respectively. The most effective strategy seemed home exercises with regular therapist follow up[Hayden2005]. It has been established that abdominal muscles and back extensors as well as gluteals become weak in the chronic low back pain and hamstrings tend to shorten[Hurtling2006,Hall1999,Vleeming2007]. Well known types of exercises that target above mentioned muscles[...] were used in this study i.e. posterior pelvic tilts, sit ups, bridging, quadruped exercises and stretches for posterior hip and knee muscles.”

12) Second paragraph under exercise therapy - restructure the sentence commencing with ‘We’ e.g. ‘All patients were given written instructions for home....’
Response:
The sentence is changed.

Outcome measures

First paragraph - restructure the sentence commencing with ‘We’ e.g. ‘Readers are referred to the design article....’

Response:
Sentence is restructured.

12) Under secondary outcome measures correct the sentence commencing ‘lumbar flexion and extension’ to include one ‘modified’

Response:
The Modified –Modified schober test (with 2 modified) is the Modified schober test which was further revised by Williams et al in 1993 and called MMST. Modified –Modified schober test is preferred over Modified schober test because of being more accurate in detecting lumbar movement because of its changed landmarks in comparison with modified schober test.[Murtagh1997,Mohseni2006]

The technique is explained in the design article.

13) Please include the manufacturer and country for the DATA LOG PC software

Response:
It is included. (Biometrics Ltd ,UK)

14) A brief description should be included in this section of the rationale for choosing pain, function and the secondary measures as the outcome measures of choice

Response:
Though completely explained in the design article, the paragraph below was added to this section:

Pain and function are arguably the 2 most fundamental clinical outcomes for low back pain [Ostelo2008]. Accurate assessment of lumbar range of motion has been recommended as a core domain in the evaluation of patients with lumbar dysfunction and monitoring treatment progress [Waddell1993, Van der Heije1997, Fritz2003]. Since the endurance of trunk muscles has been shown to be related to the incidence of low back pain, surface electromyography, specifically power spectral analysis of EMG signals has become an increasingly common method for the assessment of lumbar muscle activity and localized muscle fatigue and has been suggested as an objective safe easy and non-invasive measure for the evaluation of patients with low back pain [Mohseni-Bandpei2000].

15) References need to be incorporated into this section when referring to the Biering Sorensen test, the modified Schober test, EMG

Response:
References are added.

16) Detail needs to be included in the final paragraph explaining where electrodes were placed, and the rationale for the selection of electrode placement

Response:
It has already been explained in detail in the design article.

Data analysis

17) Please include the manufacturer and country for the SPSS software

It is done.

18) Results: First paragraph - detail the word Figure in full not Fig 1.
Response:
It is changed.

19) First paragraph - information needs to be included in this paragraph relating to which group(s) the ‘nine more patients’ were lost from

Response:
Added to the manuscript “(3 in continuous ultrasound and 6 in placebo ultrasound group)”

20) First paragraph, last sentence – replace the word ‘didn’t’ with ‘did not’

Response:
The word is replaced

21) Second paragraph, first sentence – include the word ‘years’ after mean age i.e. ‘34.7 (SD 12.6) years, with a mean pain

Response:
It is included.

22) Primary outcome measures, within group changes section – replace the word ‘in’ with ‘at’ in the final sentence to read: ‘functional ability and pain intensity at 1 month follow-up

Response:
Discussion part is totally changed and reviewer points have been addressed.

23) Secondary outcome measures – correct spelling of ‘lumbar’, and detail abbreviation SEMG

Response:
Discussion part is totally changed and reviewer points have been addressed.
24) **Figure 1** – this figure would benefit from a review of punctuation and character spacing. Also final numbers for each group at follow-up should be given at the end of the figure. The numbers under each caption should be reviewed e.g. under allocation, 25 patients are allocated to each group, however, on addition of the numbers reported under each group the commencing number is 26 (25 +1).

*Response :*

The figure is corrected.

25) **Table 1** – again this table would benefit from a review of punctuation and character spacing. No legend is included. A suggestion would also be to incorporated a column detailing analysis to compare both groups were not statistically different i.e. inclusion of P values

*Response :*

Since all of the demographic characteristics were not significantly different at base line, including a column didn’t seem relevant ,although as explained in the manuscript the effect of endurance time at baseline was further analysed.

26) **Table 2** – this table details differences between assessment times or within groups, but not between groups, perhaps a separate table might document differences between groups as these results are omitted

*Response :*

Since the analysis has changed to repeated measure ANOVA ,the table has changed subsequently .p values which were for within group differences have been removed. The effect of time and group have been incorporated in table 3.

27) Again no legend is included. No reference is made to biceps femoris for the left muscles. Please correct spelling of Illiocostalis-lumborum, and gluteus maximus
Response:

The table does not have p values so legends were no more necessary.

It has already been explained in the design article that only right biceps femoris was assessed and the eighth channel of the apparatus was connected to the digital goniometer.

28) Discussion:

Second paragraph - the authors discuss findings from Grubisic et al, however, reference is made to only having read the abstract. This would appear inappropriate and of poor scientific rigour, suggesting the reference be removed, or only included if the authors can justify its inclusion through translation of the reference

Response:

The reference is removed

29) Second paragraph – the authors make reference to ‘strong evidence that exercise is an effective treatment in CLBP’, please supply a reference to support this statement. Similarly, reference material should be included for the statement: ‘exercise programs for CLBP may be designed to reverse deconditioning ....’

Response:

From “there is strong evidence to stretching regimens ‘was from Hydaen 2005 and I had refered it after these 4 sentences to Hayden.

30) Second paragraph – the final sentence should be restructured to omit the words ‘didn’t’ and ‘we’, e.g. ‘Since the real US group did not show any improvement over that of the sham US group, improvements can only be attributed to the placebo

Response:
This sentence is deleted from discussion.

31) Third paragraph – please explain the abbreviation ‘MMS’

Response:
Modified Modified Schober test was included.

32) Sixth paragraph – please remove the word ‘couldn’t’ and replace with ‘may not’

Response:
The sentence is completely changed.

33) Sixth paragraph – please include more detail on the study by Mohensi et al. and Sung, to further substantiate the findings detailed in the manuscript

Response:
More details are included in the new version of discussion.

34) Conclusion: Please correct spelling of ‘gluteus maximus’.

Response:
The conclusions could be revised to incorporate future research ideas such as inclusion of a control non-treatment group, an exercise only group.

Response:
Conclusion is completely changed and the reviewer’s comments are addressed.

35) References: Please correct for spelling, punctuation and character spacing errors.

Response:
References are corrected.