PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A comparative study of treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial
AUTHORS	Lopez-Royo, Maria Pilar; Gómez-Trullén, Eva Maria; Ortiz-Lucas, Maria; Galán-Diaz, Rita Maria; Bataller-Cervero, Ana Vanessa; Al-Boloushi, Zaid; Hamam-Alcober, Yasmina; Herrero, Pablo

VERSION 1 - REVIEW

REVIEWER	Dr Patrick Wheeler University Hospitals of Leicester NHS Trust, UK / Loughborough University, UK No specific competing interests to declare. It is recognised that I have published a number of articles investigating treatments for different tendinopathies, and have ongoing works that have yet to be published.
REVIEW RETURNED	21-Oct-2019

GENERAL COMMENTS	The authors are to congratulated for considering a robust approach to investigating treatment options for this condition. There are some issues with English language in the written material, and I have some reservations for some of the areas of the study design and presentation. If these could be addressed or clarified these would greatly improve the quality of the manuscript. • Definition of “chronic” patella tendinopathy – from the inclusion criteria this appears to be a minimum of 3-months, which is relatively short. This needs to be clarified and explained for greater clarity to the reader. • In methods sub-heading of “studying sitting” – should this be “study setting”? • Participants – clarity is needed as to whether only proximal patella tendinopathy will be recruited, or any location of pain. • Exclusion criteria – injections with corticosteroids within 3M – clarity is needed as to whether this relates to only local injections, or an injection in any separate location • No mention in the inclusion/exclusion criteria about previous rehabilitation undertaken, is this being controlled for? • No mention in the inclusion/exclusion criteria about whether this involves recreational or professional athletes, or whether this has been considered. This is touched on in the recruitment sub-section which appears to suggest that this will be from sports clubs, but this needs to be clarified.

	• What precautions (if any) are being taken to avoid participants undergoing other treatments in addition to this study protocol during the study period. • Methods – in the 1st session participants will be instructed how to perform 3 x 15 single leg squats, on decline board. What is the process if they cannot achieve this level? More clarity about this rehabilitation plan is required. • More clarity may be required as to the participant blinding. It is not clear from the description if the participant will be adequately blinded to the procedure undertaken and what information they may be given about the expected sensations during the procedure. Greater scientific rigour would be gained if this blinding approach could be demonstrated in a pilot study, greater clarity about blinding undertaken given, or blinding assessed within-study. • In the study abstract it describes "block randomisation" in the manuscript the use of sealed envelopes, with no discussion of randomisation by blocks. This needs greater clarity • In the study "Outcomes" section, it describes data collection from a blinded assess at baseline, 10 weeks and 22 weeks after baseline. In the abstract initially there is a discussion of "three months" although this could relate to minimum symptom duration but is poorly written. In addition, measures of two weeks and 12 weeks are specified in the abstract. This apparent discrepancy needs addressing. • Maximum follow-up of 22 weeks may be too short duration to reassure readers about the longer-term outcomes, particularly as this is focusing on "chronic" patella tendinopathy. Consideration should be given to longer-term outcomes. • Assessment / outcome measures – VAS / VISA-P / SF-36. These are described with link to a reference for SF-36, but not VISA-P. Limited description is made of the "jump tests" to be undertaken, with readers directed to "table A" but no reference to other published literature, if any, that have used these same tests. Greater discussion of why specific tests were included, and potentially why others were not included, would aid clarity of understanding of the study design. • It is noted that recruitment for this study protocol is specified as starting in Oct 2018 (ie 12months ago), this is acceptable for this journal, but was thought worth noting. • In the manuscript it is stated that 17 participants per group will be recruited with an estimated drop-out rate of 20% - meaning that results are expected to be possible to be obtained from only 13-14 participants in each group. There is relatively limited data given for the power calculation, and the sample size of 17 appears to be small, especially compared to studies of PRP that have included 46 between two groups (Vetrano 2013) or a case series involving 47 patients (James 2007), or studies of ESWT using 52-62 patients between 2 groups (Thijs 2017 / Zserver 2011) Without further discussion of the power calculation it is unclear if this study may be under-powered to detect a smaller difference in outcome between groups and what steps will be taken in-study to identify if this is the case. • Statistical analysis is described, including the use of normality testing. • Some language issues, with use of lay-language at times, for example "these findings could be a breakthrough". "one the one hand, medical treatments" … • In abstract "blind assessor" should be "blinded assessor"

	• Again in abstract "… will participate in the study for a minimum of three months" – although the 3-months seems to relate to their duration of symptoms, not study follow-up. • The abstract states that "histological changes" shall be assessed – it is not clear how this is to be done. It is assumed that the authors mean "ultrasound appearances", but these are not identical.

REVIEWER	Alex Scott University of British Columbia
REVIEW RETURNED	21-Oct-2019

GENERAL COMMENTS	This statement reflects a high degree of bias among the investigators – "The expected findings could be a breakthrough for the treatment of this injury as they would allow to define the most effective treatment protocol to deal with this disease and avoid the consequences that derive from it, reflecting all of this in a new relapse prevention." Is it not also equally possible that the study will demonstrate that the treatment is ineffective? The authors cite this reference as stating that ultrasound has greater diagnostic accuracy than MRI for patellar tendinopathy, but it appears to be the wrong reference. "Ultrasound-guided sclerosis of neovessels in painful chronic patellar tendinopathy: a randomized controlled trial." Line 91 - "Many of these techniques achieve a rapid regeneration of the injured tendon." Is this statement evidence-based? This reviewer is not aware of any available treatments will result in rapid regeneration of injuried tendons. Line 106 – "…however failed to find differences between them, concluding that both technologies were equally effective". Aren't these data also consistent with a statement that both technologies were equally ineffective? It is normal to see improvement over time in patellar tendinopathy when looking at the group avereage of VISA-P scores, even in those with quite severe symptoms at first assessment. Reference 17 – it is not possible for this English-speaking reviewer to assess the accuracy of the statement that ultrasound guided percutaneous needle electrolysis is superior to ultrasound or "currents", as the reference is not available in English. If this is a key reference, could more details of the study be provided (study design, confidence intervals, etc) The scientific rationale for using electricity (3mA) to lyse tissue, over and above the mechanical action of the needle itself, is not well described. The rationale in the methods refers back to a longitudinal study without control groups - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4187605/

	Regarding the statement – “From a biological point of view, it seems reasonable to ascertain that a patient will obtain benefits thanks to the mechanical effects provided by the needle”. From this reviewers point of view, the patient could experience an injury as a result of the needle. In Dragoo et al’s study, patellar tendinopathy patients who received dry needling fared worse than such cohorts typically do (there was no improvement over time with Dry needling alone). Am J Sports Med. 2014 Mar;42(3):610-8. doi: 10.1177/0363546513518416 Will the ultrasound assessor be blinded to allocation? Can the patients be administered a questionnaire to evaluate the success of blinding? Is it accurate to call this condition a disease? (line 327)

REVIEWER	Luciana De Michelis Mendonça Universidade Federal dos Vales do Jequitinhonha e Mucuri (UFVJM) Brazil
REVIEW RETURNED	29-Oct-2019

GENERAL COMMENTS	I appreciate the opportunity to revise this manuscript. My comments aims to improve the work. Title: - I suggest to specify in the title that are needling interventions - My suggestion is to exclude the term “chronic” since there is no “acute tendinopathy”. Please see recent articles about tendinopathy… they do not specify a type… Abstract: - Line 31: If you are not specifying here about “chronic” tendinopathy, why to do in the title? - Line 35: “placebo needling” - Is this a treatment? Actually, you are comparing 2 terapies… not 3… - Why ECC and not HSR? - Line 37: What kind of jumps? VAS collected during a task? - Lines 39 – 42: I do not agree with this sentence… Why this therapies should be a “breakthrough”? And you are not investigating protocols… you are just comparing the effect of 2 therapies combined with eccentrics (additional effect)… The affirmation is too strong… - Line 49: only 2 treatments to me… Introduction: - Line 57: See my previous comment about “chronic” - In the introduction I missed some reasoning about exercises… specially because you are combining the needling therapies to eccentrics…. So should have some reasoning about this in the introduction… Methods: - Line 155: Shouldn’t be a bigger period then 48 h? Not only about the chemical effect but also psychologic effect and possible bias? - Lines 158-160: How the load progression will be implement? How you will be sure that the participants are performing properly the exercise and respecting the load progression?

	The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.

REVIEWER	joao carlos Belloti Universidade Federal de São Paulo Brazil
REVIEW RETURNED	31-Oct-2019

GENERAL COMMENTS	This RCT protocol evaluates the effectiveness of 2 needling techniques for the treatment of patellar tendinopathy. The study followed SPIRIT recommendations, however there is a need for a better description of the following points: 1- Study dates should be described as well as if study is started 2- Explain the justification and description for the sample calculation: "to detect the difference equal to or greater than 15 points on the Visa-P scale", with the reference cited (21). 3- The limitations of the study should be adequately described and discussed.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Definition of “chronic” patella tendinopathy – from the inclusion criteria this appears to be a minimum of 3-months, which is relatively short. This needs to be clarified and explained for greater clarity to the reader.

We have excluded the term “chronic” throughout the paper.

In methods sub-heading of “studying sitting” – should this be “study setting”?

Yes, it was a typo which has now been corrected.

Participants – clarity is needed as to whether only proximal patella tendinopathy will be recruited, or any location of pain.

Only proximal patella tendinopathy will be recruited, we have therefore made two changes to the manuscript:

1. History of PT and anterior knee pain located on the inferior pole of the patella for over three months; 2. Aged between 18 and 45 years; 3. Palpation tenderness of the superior insertion of the patellar tendon; 4. A score below 80 on the VISA-p questionnaire.

Exclusion criteria – injections with corticosteroids within 3M – clarity is needed as to whether this relates to only local injections, or an injection in any separate location

It refers specifically to infiltration with corticosteroids in the patellar tendon within the previous three months, therefore this has been further clarified in the text:

3. Corticosteroid injection in the patellar tendon within the previous three months.

No mention in the inclusion/exclusion criteria about previous rehabilitation undertaken, is this being controlled for?

Yes, this will be controlled for in the baseline interview, in order to determine whether it can affect the results. We have made some changes in the following sentence to clarify this:

Baseline data will include gender, age, height, weight, body-mass index, affected side, level, sports and frequency of physical activity, duration of symptoms, medication and previous rehabilitation treatments and infiltrations received.

Besides, regarding the exclusion criteria, we have included the case of patients receiving any other treatment at the time:

Exclusion criteria for the study are: 1. Knee surgery within the previous six months; 2. Chronic joint diseases; 3. Corticosteroid injection in the patellar tendon within the previous three months; 4. Contraindications for needling; 5. Use of drugs 48 hours previously (e.g. NSAIDs); 6. Any other concomitant treatment for PT.

No mention in the inclusion/exclusion criteria about whether this involves recreational or professional athletes, or whether this has been considered. This is touched on in the recruitment sub-section which appears to suggest that this will be from sports clubs, but this needs to be clarified.

It is only in amateurs. We have edited this in the text:

“high incidence of this pathology in amateur young adults”

What precautions (if any) are being taken to avoid participants undergoing other treatments in addition to this study protocol during the study period.

In the first interview, when explaining the intervention, the researcher will inform the participants that they should not receive any other treatment at the same time, and, if this were to happen, it should be communicated to the researchers, as well as any changes in medication so that this can be controlled for during the study. We will exclude patients in the case of any other treatments or infiltrations and will control for changes in medication. We have included a new sentence to make this clearer:

Participants will be asked to inform the researchers if there were any changes in medication or if they are receiving any other treatment or infiltration during the study.

Methods – in the 1st session participants will be instructed how to perform 3 x 15 single leg squats, on decline board. What is the process if they cannot achieve this level? More clarity about this rehabilitation plan is required.

Patients will perform this exercise with minimal tendon pain only and progress their speed from slow to fast, as outlined in the Curwin and Stanish protocol. We have added a sentence to make this clearer:

This will consist of performing three sets of 15 single leg squat repetitions on a decline board every day, according to Alfredson's protocol (19) increasing the speed if participants do not have pain. Participants will be informed that exercise is allowed to reach 5 in a numerical pain rating scale (20), and if it is higher then they will stop and notify the researcher, attempting once again 24 h later following the same rules.

More clarity may be required as to the participant blinding. It is not clear from the description if the participant will be adequately blinded to the procedure undertaken and what information they may be given about the expected sensations during the procedure. Greater scientific rigour would be gained if this blinding approach could be demonstrated in a pilot study, greater clarity about blinding undertaken given, or blinding assessed within-study.

We have added information about the information provided to the participants as well as how the blinding is intended via simulation of the treatment being the same procedure:

Patients will be explained that they are going to receive a needling treatment, that it may be a bit painful, and that if at any moment they are unable to tolerate the pain they must inform the researcher to stop the intervention. In order to blind patients, all the interventions were made with the ultrasound and the PNE device connected to simulate the same intervention in all groups.

We didn´t consider the need to evaluate the blinding of patients, however, we agree, this is is a good suggestion so we will add an evaluation at the end of the study via an online questionnaire. We will get in touch with the patients by email and we will ask them about which treatment they think they have received. We have added a sentence on this in the manuscript, as follows:

With the intention of evaluating patient blinding, an online questionnaire will be sent to participants upon completion of the study, asking them about the treatment they received.

In the study abstract it describes "block randomisation" in the manuscript the use of sealed envelopes, with no discussion of randomisation by blocks. This needs greater clarity.

The technique of randomization of participants is with sealed envelopes, however, the recruitment will be in blocks of fifteen (5 participants in each group), in order to better distribute all the patients among the groups. This way, we are sure that there will be no changes in therapist learning over time that will modify the treatment application.

Participants will be randomly assigned to either CG or DN-G or PNE-G with a 1:1:1 allocation using an opaque envelope, with a block size of fifteen participants (5 for each group).

In the study "Outcomes" section, it describes data collection from a blinded assess at baseline, 10 weeks and 22 weeks after baseline. In the abstract initially there is a discussion of "three months" although this could relate to minimum symptom duration but is poorly written. In addition, measures of two weeks and 12 weeks are specified in the abstract. This apparent discrepancy needs addressing.

We agree, 3 months referred to minimum duration of symptoms. However, this was confusing, therefore, we have removed it. The abstract has been rewritten according to the main text:

Participants will be assessed at baseline, at 10 weeks and at 22 weeks after baseline.

Maximum follow-up of 22 weeks may be too short duration to reassure readers about the longer-term outcomes, particularly as this is focusing on “chronic” patella tendinopathy. Consideration should be given to longer-term outcomes.

A pilot study was performed by our research group with several patients for a MSc thesis with a similar population and patients demonstrated great improvements, however they did not come back for follow-up. As this is a similar study conducted at the University we think this is a limitation as they are volunteers recruited from different places. Other studies performed at a hospital have enabled an improved follow-up, however, in this case according to our previous experience we limited the follow-up to 22 weeks to be more realistic. We have included this as a limitation.

However, there are some limitations to this study. Blinding of the physiotherapist performing the intervention is not possible. Furthermore, follow-up is limited to 22 weeks after baseline.

Assessment / outcome measures – VAS / VISA-P / SF-36. These are described with link to a reference for SF-36, but not VISA-P. Limited description is made of the “jump tests” to be undertaken, with readers directed to “table A” but no reference to other published literature, if any, that have used these same tests. Greater discussion of why specific tests were included, and potentially why others were not included, would aid clarity of understanding of the study design.

A reference has been added for the Visa-P questionnaire (Reference 19).

We included jump tests because we consider these to be a functional outcome measure for these types of patients, as most of them play sports that involve jumping. Further explanations regarding this protocol have been added to the manuscript, apart from the table A, and references have been also included to support the use of these tests:

In this evaluation, subjects will warm up during 5 minutes on a treadmill, subsequently, they will perform dynamic stretches for the leg muscles. The Jump test will be explained to participants and they will be asked to demonstrate how they will perform the assessment to ensure that they have understood it before going to the platform. Later, patients will go to the platform forces and will perform each jump 3 times (squat jump, Abalakov jump and countermovement jump test) with 60 seconds between jumps and 2 minutes between different jumps (Table A) (24-26). The maximum height of the jump will be analyzed via the measurement of the flight time recorded on the force platforms, the eccentric power and the maximum concentric force performed.

We include further details for the tests with the following explanation:

The Abalakov jump will be performed with the subject standing in an upright position with a full arm swing. A rapid downward movement will be immediately followed by a rapid upward vertical movement as high as possible, all in one sequence. The same procedure will be applied for the CMJ jump, however, this test will be performed with the hands on the hips to avoid arm swings. Finally, a Squat Jump will be performed with 90 degrees of flexion of the knee.

We have also included this text in the discussion:

Moreover, functionality of the tendon is usually measured with the VISA-p (34, 35), whereas jump tests (representing a similar action to that performed in subject’s daily sports) are only evaluated in a few papers (25, 36). Countermovement jumps and squat jumps are the most reliable and valid field tests for the estimation of the explosive power of the lower limbs in physically active men (37). Thus,

we will combine both, in order to be more accurate in the assessment of the tendon's functionality, and be able to assess changes that may affect their sport performance.

It is noted that recruitment for this study protocol is specified as starting in Oct 2018 (ie 12months ago), this is acceptable for this journal, but was thought worth noting.

Thank you for the information. Recruitment is lasting much more than expected as we do have not accessed patients from a single center, rather, we have been recruiting from different centers and inviting them to come to the University.

In the manuscript it is stated that 17 participants per group will be recruited with an estimated drop-out rate of 20% - meaning that results are expected to be possible to be obtained from only 13-14 participants in each group. There is relatively limited data given for the power calculation, and the sample size of 17 appears to be small, especially compared to studies of PRP that have included 46 between two groups (Vetrano 2013) or a case series involving 47 patients (James 2007), or studies of ESWT using 52-62 patients between 2 groups (Thijs 2017 / Zserver 2011) Without further discussion of the power calculation it is unclear if this study may be under-powered to detect a smaller difference in outcome between groups and what steps will be taken in-study to identify if this is the case.

There was an error in the sample size section, as we previously state:

A sample of 57 patients with a medical diagnosis of patellar tendinopathy will participate in this study and will be divided into three treatment groups.

Therefore, the sample size section has been corrected with 19 per group.

There was also an error with the reference, as we found the sample size calculations to be the same as in the study carried out by Scott et al (Scott A, LaPrade RF, Harmon KG, Filardo G, Kon E, Della Villa S, et al. Platelet-Rich Plasma for Patellar Tendinopathy: A Randomized Controlled Trial of Leukocyte-Rich PRP or Leukocyte-Poor PRP Versus Saline. Am J Sports Med. 2019:363546519837954.) We have changed the reference. We have also updated the reference related to SD to the one used by Scott et al. We also found 16 patients per group and 3 additional patients for drop-outs, resulting in 19. This former study also had 3 branches, similar to ours, therefore, we used it as a reference.

Statistical analysis is described, including the use of normality testing.

Some language issues, with use of lay-language at times, for example “these findings could be a breakthrough”. “one the one hand, medical treatments” …

These sentences have been rewritten.

The first group comprises medical treatments which include non-steroidal anti-inflammatory drugs (NSAIDs), platelet-rich plasma injection (4) and autologous growth factors (5). The second group

consists of physical therapies, including both conservative and invasive approaches (needling techniques).

The findings obtained may help advance the treatment of this injury…

In abstract “blind assessor” should be “blinded assessor”

Thank you for pointing this out. This was a typo, now corrected.

Again in abstract “… will participate in the study for a minimum of three months” – although the 3-months seems to relate to their duration of symptoms, not study follow-up.

Yes, it has also been corrected in the abstract to avoid confusing the reader.

A sample of 57 patients with a medical diagnosis of patellar tendinopathy will participate in this study and will be divided into three treatment groups.

The abstract states that “histological changes” shall be assessed – it is not clear how this is to be done. It is assumed that the authors mean “ultrasound appearances”, but these are not identical.

Yes. We referred to the ultrasound measures, so we have changed the words to “ultrasound appearances” as suggested.

Functionality and muscle strength parameters, pain, ultrasound appearances and patient perceived quality of life shall be evaluated using the VISA-p, jump test, VAS, US images and SF-36, respectively.

Reviewer: 2

Please leave your comments for the authors below This statement reflects a high degree of bias among the investigators – "The expected findings could be a breakthrough for the treatment of this injury as they would allow to define the most effective treatment protocol to deal with this disease and avoid the consequences that derive from it, reflecting all of this in a new relapse prevention."

Is it not also equally possible that the study will demonstrate that the treatment is ineffective?

Yes, the aim of the RCT is to analyze whether the addition of an invasive treatment may increase effectiveness, as the evidence is limited to date. According to recent publications, it seems that adding an invasive treatment may be more effective, but this has not been analyzed via a RCT in PT [12-14]. Besides, we have found studies on DN and NPE. However, none of these compared both interventions [11, 33], therefore, our aim is also to know whether the addition of a galvanic current to a DN procedure provides any additional benefits for the patient

We have also rewritten the sentence to be more conservative with our statements, as requested by the other reviewer:

The findings obtained may help advance the treatment of this injury by identifying the most effective treatment protocol and to avoid the associated consequences, such as the prevention of relapses and reducing the potential impact on the musculoskeletal system.

The authors cite this reference as stating that ultrasound has greater diagnostic accuracy than MRI for patellar tendinopathy, but it appears to be the wrong reference.

“Ultrasound-guided sclerosis of neovessels in painful chronic patellar tendinopathy: a randomized controlled trial.”

We agree, this was a mistake. This reference does not correspond with the information. We have corrected the sentence and inserted the correct reference: Stenroth L, Sefa S, Arokoski J, Toyras J. Does Magnetic Resonance Imaging Provide Superior Reliability for Achilles and Patellar Tendon Cross-Sectional Area Measurements Compared with Ultrasound Imaging? Ultrasound Med Biol. 2019;45(12):3186-98. Doi: 10.1016/j.ultrasmedbio.2019.08.001). We made some changes to the manuscript as follows:

Currently, imaging techniques, such as color-Doppler ultrasound (CD-US) and gray scale ultrasound (GS-US) can be used for the assessment of the patellar tendon to clinically confirm the diagnosis (3).

Line 91 - "Many of these techniques achieve a rapid regeneration of the injured tendon." Is this statement evidence-based? This reviewer is not aware of any available treatments will result in rapid regeneration of injuried tendons.

We have rewritten this sentence to be more conservative with this statement, as our intention was to show that it seems that these techniques could provoke a rapid regeneration, due to information from the clinical cases and case series published, however, there is no high quality research available with these techniques.

Recently, research has focused on regenerative therapies with high expectations of success because some of these techniques seem to achieve a rapid regeneration of the injured tendon (11, 12, 16).

Initially we only included clinical studies as references, however, based on this review we have included a study with animals to support needling interventions in tendons [16]. In this paper, the following results and conclusions are reported:

“Both the mild and moderate needling groups caused a transient healing response at early time points as shown by a statistically significant ($p < 0.05$) reduction in mechanical properties, and increase in blood flow, inflammation, and production of collagen III and glycosaminoglycans as compared to the control. Furthermore, mild needling properties returned to or exceeded pre-needling values at the 6-week time point. Clinical significance: Needling the rat supraspinatus tendon is a feasible technique that causes a transient healing response followed by a return to, or improvement of, normal tendon properties, indicating potential applicability in understanding the effects of current practices utilizing dry needling of tendons in humans”

Line 106 – "…however failed to find differences between them, concluding that both technologies were equally effective". Aren't these data also consistent with a statement that both technologies were equally ineffective? It is normal to see improvement over time in patellar tendinopathy when looking at the group avereage of VISA-P scores, even in those with quite severe symptoms at first assessment.

The cited reference states that both therapies are effective and because of this, we have used this term. We agree that the normal evolution of the PT may increase VISA-p values however, from this study this cannot be concluded, as it is limited to these two interventions. The reason we cite this reference was to show the comparison between two common techniques, one of these DN, to support our study. There are more studies however they do not include DN. Therefore, we chose this reference. However, we are aware that the problem of the many studies of DN or PNE available is that they compare two invasive techniques but they do not include a control group, as we propose with only an exercise intervention, therefore, for this reason we designed this study including three branches.

Reference 17 – it is not possible for this English-speaking reviewer to assess the accuracy of the statement that ultrasound guided percutaneous needle electrolysis is superior to ultrasound or "currents", as the reference is not available in English. If this is a key reference, could more details of the study be provided (study design, confidence intervals, etc)

This reference is not especially relevant. We realized that this paper, apart from being available only in Spanish, is not a peer reviewed publication, therefore, we have decided to remove it from the reference list and deleted the sentence associated to it.

The scientific rationale for using electricity (3mA) to lyse tissue, over and above the mechanical action of the needle itself, is not well described. The rationale in the methods refers back to a longitudinal study without control groups - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4187605/

A rationale is provided at the end of the introduction, as a hypothesis.

From a biological point of view, it seems reasonable to hypothesize that a patient will obtain benefits thanks to the mechanical effects provided by the needle, and that patients may benefit more if the electrolysis effect is added to the mechanical stimuli provided by the needle (16).

Intratissue percutaneous electrolysis (PNE) is a new technique that is being used increasingly in daily clinical practice despite not having comparative RCTs to support the theoretical superior effectiveness of the same. Considering this, one of the aims of this study is to investigate if this theoretical rationale may be supported by scientific evidence or not, as the design will allow the possibility to analyze whether adding the electrical current provides an additional benefit to DN:

Therefore, the aim of this study is to determine whether invasive techniques have additional effects for the treatment of PT when compared with EE alone, and whether the application of PNE provides any additional benefits aside from performing DN alone, in the short and long term.

However, we realized that the decision to include the dose of 3mA does not seem to be clear, therefore we have included an explanation in the methods section supported by reference 18:

The dose of 3 mA has demonstrated to be as effective as 6 mA in the treatment of tendinopathy injuries in animal models (18) as a result, the lower dose was selected for this study.

Regarding the dose, a study in patellar tendinopathy in a mouse model (doi: 10.1016/j.recot.2014.01.002) studied 4 groups: the control group, collagenase group, and two PNE technique treatment groups of 3 and 6 mA, respectively. PNE produced an increase in anti-inflammatory and angiogenic molecular mechanisms. Since both treatments/dosages were equally effective, 3 mA has been used as it is better tolerated by patients and less aggressive. Also in plantar fasciosis there is a RCT that compared PNE and corticosteroids injection. Both treatments were effective and for the group of PNE the doses applied were also 3 mA (Iborra- Marcoss A. et al. 2018; doi: 10.1177/1071100718754421). Based on the aforementioned explanations, we have added this reasoning in the manuscript text.

Regarding the statement – “From a biological point of view, it seems reasonable to ascertain that a patient will obtain benefits thanks to the mechanical effects provided by the needle”. From this reviewers point of view, the patient could experience an injury as a result of the needle. In Dragoo et al’s study, patellar tendinopathy patients who received dry needling fared worse than such cohorts typically do (there was no improvement over time with Dry needling alone). Am J Sports Med. 2014 Mar;42(3):610-8. doi: 10.1177/0363546513518416

We do not agree with DN being worse, because at 26 weeks, in the cited paper comparing PRP and DN, both groups improved, with no differences between them:

“at ≥26 weeks, the scores improved by 33.2 ± 14.0 points (P = .001) in the DN group (n = 9) and by 28.9 ± 25.2 points (P = .01) in the PRP group (n = 7)”

We have added a reference of a study with animals to further support this statement. In this study, published by Riggin et al. the results were:

“Both the mild and moderate needling groups caused a transient healing response at early time points as shown by a statistically significant ($p < 0.05$) reduction in mechanical properties, and increase in blood flow, inflammation, and production of collagen III and glycosaminoglycans as compared to the control. Furthermore, mild needling properties returned to or exceeded pre-needling values at the 6-week time point. Clinical significance: Needling the rat supraspinatus

tendon is a feasible technique that causes a transient healing response followed by a return to, or improvement of, normal tendon properties, indicating potential applicability in understanding the effects of current practices utilizing dry needling of tendons in humans.”

Will the ultrasound assessor be blinded to allocation? Can the patients be administered a questionnaire to evaluate the success of blinding?

The ultrasound assessor will be the same for the rest of assessments and she will be blinded.

We did not consider the need to evaluate the blinding of patients, however, we agree, this is a good suggestion, therefore we will add an evaluation at the end of the study via an online questionnaire.

We will get in touch with the patients by email and they will be asked about what treatment they think they have received. We have added a sentence on this in the manuscript:

With the intention of evaluating patient blinding, an online questionnaire will be sent to participants upon completion of the study, asking them about the treatment they received.

Is it accurate to call this condition a disease? (line 327)

We have reviewed the manuscript and changed this to:

PT is a common cause of knee pain in cases of degeneration of the patellar tendon.

Reviewer: 3

I suggest to specify in the title that are needling interventions

Not all the interventions involve needling, because in one of the groups, the intervention is a sham needle plus exercise protocol (Control group). Therefore, we believe that by writing “needling intervention” this may be confusing and not accurate, as we also compare it with a control group.

My suggestion is to exclude the term “chronic” since there is no “acute tendinopathy”. Please see recent articles about tendinopathy… they do not specify a type…

We agree, we have updated the use of terms throughout the entire manuscript.

Abstract:

Line 31: If you are not specifying here about “chronic” tendinopathy, why to do in the title?

Changed.

Line 35: “placebo needling” - Is this a treatment? Actually, you are comparing 2 terapies… not 3…

The intervention will be performed in all groups with physical exercise, in addition, two of them will receive needling techniques, however the third group also receives an intervention based on an exercise program only.

Why ECC and not HSR?

We think both ECC and HSR could have been included for patellar tendinopathy rehabilitation as ECC and HSR both obtained very good results in the short-term and follow-up in previous research studies (Kongsgaard et al, 2009; Kingma JJ et al. 2007; Magnussen RA et al. 2009; Malliaras P et al. 2013; Sussmilch-Leitch SP et al. 2012) that evaluated the functionality (our first outcome).

We decided to include the ECC because of two reasons: first, because ECC has been the most investigated up to date; second, because in protocols with HSR it is necessary to perform more supervision during all the treatment as they should change the weight depending on the estimated one-repetition maximum (1RM) and also some equipment is necessary. With the ECC, the patients

can do the same exercise on all days without confusion, therefore, we decided to use this as it was easier to standardize for the whole sample.

Line 37: What kind of jumps? VAS collected during a task?

The jump test has been described in the text, as suggested also by the other reviewer:

In this evaluation, subjects will warm up during 5 minutes on a treadmill, subsequently, they will perform dynamic stretches for the leg muscles. The Jump test will be explained to participants and they will be asked to demonstrate how they will perform the assessment to ensure that they have understood it before going to the platform. Later, patients will go to the platform forces and will perform each jump 3 times (squat jump, Abalakov jump and countermovement jump test) with 60 seconds between jumps and 2 minutes between different jumps (Table A) (24-26). The maximum height of the jump will be analyzed via the measurement of the flight time recorded on the force platforms, the eccentric power and the maximum concentric force performed.

We include further details for the tests with the following explanation:

The Abalakov jump will be performed with the subject standing in an upright position with a full arm swing. A fast downward movement will be immediately followed by a fast upward vertical movement as high as possible, all in one sequence. The same procedure will be applied for the CMJ jump, however, this test will be performed with the hands on the hips to avoid arm swings. Finally, the Squat Jump will be performed with 90 degrees of flexion of the knee.

We have also included this in the discussion

Moreover, functionality of the tendon is usually measured with the VISA-p (34, 35), whereas jump tests (representing a similar action to that performed in subject's daily sports) are only evaluated in a few papers (25, 36). Countermovement jumps and squat jumps are the most reliable and valid field tests for the estimation of the explosive power of the lower limbs in physically active men (37). Thus, we will combine both, in order to be more accurate in the assessment of the tendon's functionality, and be able to assess changes that may affect their sport performance.

In the material and methods section, we specify that the VAS was not asked during the jump test:

"participants will complete the Visual Analogical Scale (VAS), considering the level of pain they feel while practicing their sport's activity"

Lines 39 – 42: I do not agree with this sentence… Why this therapies should be a "breakthrough"? And you are not investigating protocols… you are just comparing the effect of 2 therapies combined with eccentrics (additional effect)… The affirmation is too strong…

We have edited this. This was a translation error. What we wanted to explain was that this study will help advance understanding on the effectiveness of two needling treatments for PT. We have rephrased the text as follows:

The expected findings will allow us to advance in the treatment of this injury as they will help determine whether a needling intervention has additional effects on an eccentric exercise program and whether any of the needling modalities is more effective than the other.

Line 49: only 2 treatments to me…

This is also edited with the changes in the paragraph above.

Line 57: See my previous comment about “chronic”

Changed throughout the entire manuscript.

In the introduction I missed some reasoning about exercises… specially because you are combining the needling therapies to eccentrics…. So should have some reasoning about this in the introduction…

The idea of our study is to combine the “gold standard conservative treatment” with placebo, DN or PNE, in order to know if the needling techniques has any additional benefit and if there are differences between them. We have added information to one of the intro paragraphs to show the reasoning behind the use of this exercise, although, concretely, we chose EE:

Conservative therapies are generally accepted as the first line of approach for managing PT (6, 7), considering exercise as the gold standard of treatment, either eccentric exercise (EE) or high slow resistance training programs. Both had demonstrated similar effectiveness in the treatment of PT (6-8). In 2012, EE was shown to be effective in the treatment of tendinopathies at various locations of the body, including PT, and there was a greater likelihood of clinical improvement when performed on a declined surface (6, 8, 9). In recent years, further evidence now supports the fact that exercise is more effective than other conventional treatments in tendinopathy, such as iontophoresis, US, Cyriax treatment, etc. (10).

Methods:

Line 155: Shouldn’t be a bigger period then 48 h? Not only about the chemical effect but also psychologic effect and possible bias?

We followed the recommendations of the medical doctor participating in the study, who considered that these drugs do not have effects after 48 h.

Lines 158-160: How the load progression will be implement? How you will be sure that the participants are performing properly the exercise and respecting the load progression?

Patients will do this exercise with minimal tendon pain only and progress their speed from slow to fast, as outlined in the Curwin and Stanish protocol. We have added a sentence to make this clearer:

This will consist of performing three sets of 15 single leg squat repetitions on a decline board every day, according to Alfredson’s protocol (19) increasing the speed if participants do not have pain. Participants will be informed that exercise is allowed to reach 5 in a numerical pain rating scale (20),

and if it is higher then they will stop and notify the researcher, attempting once again 24 h later following the same rules.

Reviewer: 4

Study dates should be described as well as if study is started.

In page 11 we wrote: “Recruitment of subjects for the trial will take place between October 2018 and March 2020 and will be carried out by means of informative campaigns targeted at different Sports Clubs and Federations by means of e-mail and advertisements in the different University mass media”. With this sentence, we understand that it is clear that study has commenced, and that this is still ongoing until March 2020.

Explain the justification and description for the sample calculation: "to detect the difference equal to or greater than 15 points on the Visa-P scale", with the reference cited (21).

There was an error in the sample size section regarding the number of patients, as previously we explained that:

A sample of 57 patients with a medical diagnosis of patellar tendinopathy will participate in this study and will be divided into three treatment groups.

Therefore, the sample size section has been corrected with 19 per group. There was also an error regarding the reference, as we found the sample size calculations to be the same as in the study carried out by Scott et al (Scott A, LaPrade RF, Harmon KG, Filardo G, Kon E, Della Villa S, et al. Platelet-Rich Plasma for Patellar Tendinopathy: A Randomized Controlled Trial of Leukocyte-Rich PRP or Leukocyte-Poor PRP Versus Saline. Am J Sports Med. 2019:363546519837954.) We have changed the reference. We have also updated the reference regarding SD to the one used by Scott et al. We also found 16 patients per group and 3 additional patients for drop-outs, resulting in 19. This is also a study with 3 branches similar to ours so we used it as a reference.

The limitations of the study should be adequately described and discussed.

Following the suggestions by other reviewers, we have included a few more limitations to our study:

However, there are some limitations to this study. Blinding of the physiotherapist performing the intervention is not possible. Furthermore, follow-up is limited to 22 weeks after baseline.

VERSION 2 – REVIEW

REVIEWER	Luciana De Michelis Mendonça UFVJM Brazil
REVIEW RETURNED	19-Nov-2019

GENERAL COMMENTS	I keep my statement that the authors are not investigating the effect of 3 treatments… The EE group are playing a "control group role"… because the 3 groups have done EE…Which is the “placebo group” for exercise alone? So, this study compares the aditional effect of 2 interventions … The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.

REVIEWER	joao carlos Belloti Escola Paulista de Medicina - Universidade Federal de São Paulo Brazil
REVIEW RETURNED	20-Dec-2019

GENERAL COMMENTS	The authors have made the requested corrections and the protocol is suitable for publication.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 3

Please leave your comments for the authors below I keep my statement that the authors are not investigating the effect of 3 treatments… The EE group are playing a "control group role"… because the 3 groups have done EE…Which is the “placebo group” for exercise alone? So, this study compares the aditional effect of 2 interventions …

In our protocol we defined 3 intervention groups, all of which will receive a treatment: 1) EE+ sham needle, 2) EE+ DN and 3) EE+PNE. In fact, the statement regarding the comparison between three treatments was something specifically requested when we applied to the ethical committee, as it cannot be considered a placebo (this would be the case if we would have only performed sham DN but not adding the gold standard treatment with EE). Therefore, we agree with the reviewer that all of groups receive the gold standard treatment (EE) and this allows us to study if there are any additional effects for the use of DN or PNE, however, we think that the group not receiving invasive therapy should be considered as an intervention group because they received a real treatment. Because of this we have rewritten the paragraph explaining the study aim, as follows:

Therefore, the aim of this study is to determine which intervention is the most effective, and whether invasive techniques have additional effects for the treatment of PT when compared with EE alone. Moreover, whether the application of PNE provides any additional benefits aside from performing DN alone, in the short and long term.

VERSION 3 - REVIEW

REVIEWER	Luciana De Michelis Mendonça UFVJM Brazil
REVIEW RETURNED	13-Jan-2020

GENERAL COMMENTS	I have only 2 suggestions:

	Title: change " A comparative study of three treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial" to "A comparative study of treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial" because you are not assessing the effect of EE, since you do not have a control group. So, I suggest to exclude the word "three". Objective : change " Therefore, the aim of this study is to determine which intervention is the most effective, and whether invasive techniques have additional effects for the treatment of PT when compared with EE alone. Moreover, whether the application of PNE provides any additional benefits aside from performing DN alone, in the short and long term." to "Therefore, the aim of this study is to determine the additional effect of two interventions combined with EE and compare which one is the most effective at short and long-term follow-up for patients with PT.". The authors made an improvement, I just adjust to make it clearer... The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.

VERSION 3 – AUTHOR RESPONSE

Reviewer: 3

Title: change " A comparative study of three treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial" to "A comparative study of treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial" because you are not assessing the effect of EE, since you do not have a control group. So, I suggest to exclude the word "three".

Objective : change " Therefore, the aim of this study is to determine which intervention is the most effective, and whether invasive techniques have additional effects for the treatment of PT when compared with EE alone. Moreover, whether the application of PNE provides any additional benefits aside from performing DN alone, in the short and long term." to "Therefore, the aim of this study is to determine the additional effect of two interventions combined with EE and compare which one is the most effective at short and long-term follow-up for patients with PT.". The authors made an improvement, I just adjust to make it clearer...

Thank you very much for your comments. We are agree with your opinion and we have changed the title and the objective as you suggest.

We have excluded the term "three" in the title.

A comparative study of treatment interventions for patellar tendinopathy: a protocol for a randomized controlled trial

We have made some changes in the objective to clarify this:

Therefore, the aim of this study is to determine the additional effect of two interventions combined with EE and compare which one is the most effective at short and long-term follow-up for patients with PT.

VERSION 4 - REVIEW

REVIEWER	Luciana De Michelis Mendonça UFVJM Brazil
REVIEW RETURNED	21-Jan-2020

GENERAL COMMENTS	The authors just need to change the objective of the abstract to be the same as in the manuscript . The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.