PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	NEUROCANTRIAL: Study Protocol for a Randomized Controlled Trial of a Pain Neuroscience Education Program in Adults with Cancer Pain
AUTHORS	Ordoñez-Mora, Leidy; Rosero, Ilem; Morales-Osorio, Marco; Guil, Rocío; Quintero Jordan, Giancarlo; Agudelo Jimenez, Julian; Gonzalez-Ruiz, Katherine; Avila-Valencia, Juan

VERSION 1 – REVIEW

REVIEWER	Lahousse, Astrid Vrije Universiteit Brussel, Physical therapist and rehabilitation science
REVIEW RETURNED	30-Jan-2023

GENERAL COMMENTS	Dear Authors, Thank you for sending this study protocol entitled: « Study protocol for a randomized controlled trial of pain neuroscience education program in adults with cancer pain». This manuscript points out an important shortcoming in oncological care and describes a novel intervention that has never been investigated in cancer patients (stage III and IV) before. The protocol has been developed with patients, which underlines once more the importance of tackling this issue. I read it with interest, and I'm looking forward to the results. However, I have a few comments for you below. Major comments: Comment 1: Eligibility criteria: You mentioned in the title of the paper "adults with cancer pain". However, you are not mentioning it in the inclusion criteria. How will you screen patients for pain? Usually, it is advised to have a minimum pain of 3-4 out of 10 on the BPI or P-VAS scale at screening. Can you please provide more information in the manuscript and elaborate on why you did not add this criterion? This information is important because I don't think that late-stage / palliative patients without or with little pain will find added value in following nine PNE sessions. Comment 2: Eligibility criteria: How do you deal with other chronic pain comorbidities? Such as rheumatoid arthritis, and fibromyalgia, which were present before cancer/cancer treatment. Comment 3: Analyses: I would strongly advise performing further analyses on medication usage during the intervention period (how much pain medication, how strong). Minor comments:

	Comment 1: Abstract: the quality of the writing of the abstract could be better. You should reformulate/rewrite the introduction, methods, and ethical considerations parts to a higher quality. Comment 2: Abstract: specify shortly what is the content/format of conventional management. Comment 3: Abstract: please add your research hypotheses to the abstract. Comment 4: Abstract: methods: can you please add how long the intervention will be (10 weeks?) Comment 5: Abstract: methods: can you please add when the patients will be measured? Baseline, post, follow-ups? Comment 6: Abstract: methods: can you please mention what is the primary outcome? Comment 7: Abstract: methods: can you please add that the auteurs are committed to reporting the results to peer-reviewed journals? Comment 8: Introduction: The EduCan trail recently shared some of their finds. See DOI: 10.1002/ar.25127 Comment 9: Eligibility criteria: why are 11 years of education relevant? Comment 10: Eligibility criteria: are patients excluded if they cannot speak or read Spanish? Or will you provide the PNE in several languages? Comment 11: Eligibility criteria: What is the minimum age? 18 years old? Comment 12: Participant selection, recruitment, and consent: Please correct the verb tense of this text part. Example: “Participants were identified” to “participants are / will be identified……” Comment 13: Sample size: I performed your sample size calculation in “Gpower 3.1.”. I did not reach the same number of subjects. Can you please explain which program you use and if it is one- or two-tailed? Comment 14: Allocation and randomization: Please elaborate on why are you not performing strata randomization based on recruitment location (pain medicine or palliative care ward). Comment 15: Masking: I think that the term “Blinding” is a more appropriate term for the title “masking”? Comment 16: Intervention group: instead of “biology and physiology,” use “on a biopsychosocial manner”.

	Comment 17: Results: I think that the term “Outcomes” is a more appropriate term for the title “Results”? Comment 18: Secondary measures: remove “The Central Sensitization Inventory is used for determining central sensitization.”. By only using the CSI, you cannot determine if the patient has CS, but you can identify symptoms related to CS. Please remove the first sentence. Comment 19: Secondary measures: same comment by only using the DN4, you cannot determine neuropathic pain. Additional tests are needed, but the DN4 can identify symptoms related to neuropathic pain.

REVIEWER	Salazar-Méndez , Joaquín Universidad Santo Tomás, Escuela de Kinesiología, Facultad de Salud
REVIEW RETURNED	22-Feb-2023

GENERAL COMMENTS	Excellent research proposal, innovative and of great clinical relevance. Only minor changes to the manuscript should be considered, which are detailed in the file I have attached. Congratulations on the theme you are going to address. It is a therapeutic modality that has barely been investigated in the cancer population, so the research presents great innovation and has enormous relevance both in the field of research and in the clinical field. I have some comments that would improve the manuscript and clarify some points that are not very understandable. In general, they do not affect the purpose of the investigation, rather they are addressed as constructive criticism. #1.- In the abstract they indicate that the PNE lasts 30 minutes, but in the intervention group section they mention 30-40 minutes. #2.- In the first paragraph of the introduction I suggest better connecting the different ideas that were embodied since these are pertinent, but adequate cohesion in the writing is not visualized. Specifically, what was written in citation 2 could be improved, and what is related to nociceptive, neuropathic and nociplastic mechanisms. It would be interesting to integrate the relationship of these mechanisms with cancer pain due to cancer treatment. #3.- According to the eligibility criteria, male patients with prostate cancer and women with genitourinary cancer will be included. Considering this, nothing specific to prostate or genitourinary cancer is displayed in the introduction, so I suggest indicating aspects related to these specific cancers (e.g. epidemiology), thus giving the research a better context and guiding the reader. #4.- In the third introductory paragraph it is mentioned: “In the future, studies are required to evaluate these new treatment approaches that include educational aspects within the intervention process”. This sentence is extremely relevant because it precedes the intervention that is intended to be carried out in this investigation. However, it lacks cohesion and strength to give relevance and importance to education in these patients. Therefore, I suggest changing the wording so that the importance of education is understood, specifically of the PNE.

	#5.- In the fourth paragraph of the introduction, I don't see it as necessary to name the titles of the studies, just cite them. Doing this would reduce the number of words in the introduction, making it more readable. If the reader is interested in going to read these cited articles, they will go to the references to be able to view them. #6.-in the last paragraph of the introduction I suggest indicating the population (men with prostate cancer and women with genitourinary cancer) in the objective. This gives context to the reader who is interested in the investigation. #7.- In trial design and context (line 47-48) I suggest being more specific with blinding. Single blind is mentioned in the introduction; in allocation and randomization it is mentioned that the statistical analysis will be blinded, in masking it is indicated that the principal investigator will be blinded. I suggest being clearer. #8.- In eligibility criteria (line 8). Abbreviation TNM is not previously described in the text. #9.- The first inclusion criterion (line 13) indicates that patients with a life expectancy of more than 3 months (more than 12 weeks) will be admitted and the intervention lasts 2 and a half months (10 weeks). They may be very tight in the evaluation times considering that there is a possibility that in certain weeks some participants will not be able to attend, so that the final session could be very close to an eventual loss due to death. I understand that they will do an intention-to-treat analysis, but I am equally concerned about the temporality, so I suggest re-analyzing this aspect to avoid very high loss rates. #10.- in Sample size (line 5) indicate “we will use the results of the preliminary study by Manfuku”. This should be written in the past tense since the sample size calculation has already been done. #11.- In sample size I interpret that they used the mean difference between two groups to calculate the sample size. It may be important to specifically indicate the test used for the determination of the number of subjects. #12.- In the intervention group section it is not clear what the treatment session will be like. Will it be individual? group? The information will be delivered through PowerPoint? Will the issues be allowed to be discussed between the dealer and the participants? Will it be passive or active learning? Will the information be channeled through metaphors (they are only mentioned in the abstract)? Will it be directed towards cancer pain, or will it be general? #13.- In results (line 39-40) they indicate: “, an assessment at baseline and 10 weeks after the intervention is considered”. This can be interpreted as the second evaluation will be carried out 10 weeks after finishing the last PNE session. will it be so? Or will the second evaluation be immediately after the intervention (week 10 of the study)? This could be clarified by attaching a figure like the following: “Flow diagram of the planned protocol pathway”. (I don't know if they have it done, I don't have access to that) #14.- In the data analysis (line 45-46) it is indicated that quality of life and physical function will be considered primary variables, but in the results section, it is mentioned that they are secondary variables.

REVIEWER	Gargallo, Pedro Catholic University of Valencia Saint Vincent Martyr, Physioteraphy
REVIEW RETURNED	28-Feb-2023

GENERAL COMMENTS	Dear authors, Firstly, I would like to congratulate you on the quality of the protocol you have developed, since it meets all the quality criteria and the research plan is clearly laid out. My opinion is that the work only requires a few minor modifications, which are reflected in the attached document. ABSTRACT SECTION: - What is the meaning of conventional treatment? Specify the type of treatment (exercise, exercise + nutrition, pharmacological, etc) - Sample size calculation: see the protocols in the literature ((a sample size calculation was performed based on the medical histories of 80 adults presenting with oncologic pain))?? - When you refer “After the baseline assessment process,randomization, allocation concealment, and masking will be performed at different stages” which is the meaning of “different stages”. It refers to a different stages of the cancer or a different stages of the study period? Specify. - Limitations have not been included in the study by the authors, only strength points. Please. Add limitations of the study. INTRODUCTION SECTION: - At the end of the introduction, add the population and the main hypothesis: “Therefore, the present study aims to examine the effectiveness of PNE in relation to pain, biopsychosocial variables, and functional capacity compared with conventional management on X population”. The main hypotheses proposed are … METHODS AND ANALYSIS SECTION: - Very complete and adequate report. DATA ANALYSIS SECTION: - Declaration It is necessary to update to the 2020 CONSORT Declaration version

VERSION 1 – AUTHOR RESPONSE

Revisor 1
Dear Authors,
Thank you for sending this study protocol entitled: « Study protocol for a randomized controlled trial of pain neuroscience education program in adults with cancer pain». This manuscript points out an important shortcoming in oncological care and describes a novel intervention that has never been investigated in cancer patients (stage III and IV) before. The protocol has been developed with patients, which underlines once more the importance of tackling this issue. I read it with interest, and I’m looking forward to the results. However, I have a few comments for you below.
Major comments:

Comment 1: Eligibility criteria: You mentioned in the title of the paper “adults with cancer pain”. However, you are not mentioning it in the inclusion criteria. How will you screen patients for pain? Usually, it is advised to have a minimum pain of 3-4 out of 10 on the BPI or P-VAS scale at screening. Can you please provide more information in the manuscript and elaborate on why you did not add this criterion? This information is important because I don’t think that late-stage / palliative patients without or with little pain will find added value in following nine PNE sessions.
RESPONSE: The observation is appreciated since it is not included in the text; it was defined to include patients with pain with a score higher than 3, but upon review, it is not explicit in the article.
Comment 2: Eligibility criteria: How do you deal with other chronic pain comorbidities? Such as rheumatoid arthritis, and fibromyalgia, which were present before cancer/cancer treatment.
RESPONSE: This clarification is included in the exclusion criteria.
Comment 3: Analyses: I would strongly advise performing further analyses on medication usage during the intervention period (how much pain medication, how strong).
RESPONSE: Follow-up of pain medications is planned, including type, dosage, schedules of consumption, and if there are any modifications during the sessions. is included in the text.
Minor comments:
Comment 1: Abstract: the quality of the writing of the abstract could be better. You should reformulate/rewrite the introduction, methods, and ethical considerations parts to a higher quality.
RESPONSE: Revised and redrafted.
Comment 2: Abstract: specify shortly what is the content/format of conventional management.
RESPONSE: Done
Comment 3: Abstract: please add your research hypotheses to the abstract.
RESPONSE: Done
Comment 4: Abstract: methods: can you please add how long the intervention will be (10 weeks?)
RESPONSE: Done
Comment 5: Abstract: methods: can you please add when the patients will be measured? Baseline, post, follow-ups?
RESPONSE: Done
Comment 6: Abstract: methods: can you please mention what is the primary outcome?
RESPONSE: Done
Comment 7: Abstract: methods: can you please add that the auteurs are committed to reporting the results to peer-reviewed journals?
RESPONSE: Done
Comment 8: Introduction: The EduCan trail recently shared some of their finds. See à DOI: 10.1002/ar.25127
Comment 9: Eligibility criteria: why are 11 years of education relevant?
RESPONSE: It had been proposed because of the type of intervention, since the conceptualization of nerves, spinal cord, and brain was considered relevant; however, this item was reviewed and, based on the antecedent, it was withdrawn, leaving the base score with the MOCA scale as the only criterion.
Comment 10: Eligibility criteria: are patients excluded if they cannot speak or read Spanish? Or will you provide the PNE in several languages?
RESPONSE: We will only work with patients who are fluent in Spanish, since this criterion is established due to the conditions of the intervention and in order to generate effective feedback.
Comment 11: Eligibility criteria: What is the minimum age? 18 years old?
RESPONSE: Included in the text
Comment 12: Participant selection, recruitment, and consent: Please correct the verb tense of this text part. Example: “Participants were identified” to “participants are / will be identified……”
RESPONSE: Done
Comment 13: Sample size: I performed your sample size calculation in “Gpower 3.1.”. I did not reach the same number of subjects. Can you please explain which program you use and if it is one- or two tailed?

RESPONSE: The correction was made in the data placed since the observation of the pair is in accordance with the rectification.
Comment 14: Allocation and randomization: Please elaborate on why are you not performing strata randomization based on recruitment location (pain medicine or palliative care ward).
RESPONSE: All patients are recruited in the same place that corresponds to the outpatient consultation in the palliative care unit.
Comment 15: Masking: I think that the term “Blinding” is a more appropriate term for the title “masking”?
RESPONSE: The correction is due to the adoption in Spanish of the term enmascaramiento “masking” instead of cegamiento “blinding”.
Comment 16: Intervention group: instead of “biology and physiology,” use “on a biopsychosocial manner”.
RESPONSE: Done
Comment 17: Results: I think that the term “Outcomes” is a more appropriate term for the title “Results”?
RESPONSE: Done
Comment 18: Secondary measures: remove “The Central Sensitization Inventory is used for determining central sensitization.”. By only using the CSI, you cannot determine if the patient has CS, but you can identify symptoms related to CS. Please remove the first sentence.
RESPONSE: Done
Comment 19: Secondary measures: same comment by only using the DN4, you cannot determine neuropathic pain. Additional tests are needed, but the DN4 can identify symptoms related to neuropathic pain.
RESPONSE: Done

REVIEWER 2
Congratulations on the theme you are going to address. It is a therapeutic modality that has barely been investigated in the cancer population, so the research presents great innovation and has enormous relevance both in the field of research and in the clinical field. I have some comments that would improve the manuscript and clarify some points that are not very understandable. In general, they do not affect the purpose of the investigation, rather they are addressed as constructive criticism.

#1.- In the abstract they indicate that the PNE lasts 30 minutes, but in the intervention group section they mention 30-40 minutes.
RESPONSE: Done
#2.- In the first paragraph of the introduction I suggest better connecting the different ideas that were embodied since these are pertinent, but adequate cohesion in the writing is not visualized. Specifically, what was written in citation 2 could be improved, and what is related to nociceptive, neuropathic and nociplastic mechanisms. It would be interesting to integrate the relationship of these mechanisms with cancer pain due to cancer treatment.
RESPONSE: Done
#3.- According to the eligibility criteria, male patients with prostate cancer and women with genitourinary cancer will be included. Considering this, nothing specific to prostate or genitourinary cancer is displayed in the introduction, so I suggest indicating aspects related to these specific cancers (e.g. epidemiology), thus giving the research a better context and guiding the reader.
RESPONSE: Done
#4.- In the third introductory paragraph it is mentioned: “In the future, studies are required to evaluate these new treatment approaches that include educational aspects within the intervention process”. This sentence is extremely relevant because it precedes the intervention that is intended to be carried out in this investigation. However, it lacks

cohesion and strength to give relevance and importance to education in these patients. Therefore, I suggest changing the wording so that the importance of education is understood, specifically of the PNE.
RESPONSE: Adjusted for clarity.
#5.- In the fourth paragraph of the introduction, I don't see it as necessary to name the titles of the studies, just cite them. Doing this would reduce the number of words in the introduction, making it more readable. If the reader is interested in going to read these cited articles, they will go to the references to be able to view them.
RESPONSE: Done
#6.-in the last paragraph of the introduction I suggest indicating the population (men with prostate cancer and women with genitourinary cancer) in the objective. This gives context to the reader who is interested in the investigation.
RESPONSE: Done
#7.- In trial design and context (line 47-48) I suggest being more specific with blinding. Single blind is mentioned in the introduction; in allocation and randomization it is mentioned that the statistical analysis will be blinded, in masking it is indicated that the principal investigator will be blinded. I suggest being clearer.
RESPONSE: The review was done and it is considered that in the text it is clear that both the investigator and the evaluations are blinded.
#8.- In eligibility criteria (line 8). Abbreviation TNM is not previously described in the text.
RESPONSE: Done
#9.- The first inclusion criterion (line 13) indicates that patients with a life expectancy of more than 3 months (more than 12 weeks) will be admitted and the intervention lasts 2 and a half months (10 weeks). They may be very tight in the evaluation times considering that there is a possibility that in certain weeks some participants will not be able to attend, so that the final session could be very close to an eventual loss due to death. I understand that they will do an intention-to-treat analysis, but I am equally concerned about the temporality, so I suggest re-analyzing this aspect to avoid very high loss rates.
RESPONSE: A life expectancy greater than this time is being worked on, so it is considered that the established times are in accordance with the first evaluation and the second 10 weeks.
#10.- in Sample size (line 5) indicate “we will use the results of the preliminary study by Manfuku”. This should be written in the past tense since the sample size calculation has already been done.
RESPONSE: Done
#11.- In sample size I interpret that they used the mean difference between two groups to calculate the sample size. It may be important to specifically indicate the test used for the determination of the number of subjects.
RESPONSE: It was included, and the adjustments suggested by another peer in this regard were made.
#12.- In the intervention group section it is not clear what the treatment session will be like. Will it be individual? group? The information will be delivered through PowerPoint? Will the issues be allowed to be discussed between the dealer and the participants? Will it be passive or active learning? Will the information be channeled through metaphors (they are only mentioned in the abstract)? Will it be directed towards cancer pain, or will it be general?
RESPONSE: Done
#13.- In results (line 39-40) they indicate: “, an assessment at baseline and 10 weeks after the intervention is considered”. This can be interpreted as the second evaluation will be carried out 10 weeks after finishing the last PNE session. will it be so? Or will the second evaluation be immediately after the intervention (week 10 of the study)? This could be clarified by attaching a figure like the following: “Flow diagram of the planned protocol pathway”. (I don't know if they have it done, I don't have access to that)
RESPONSE: Included as supplementary material

REVIEWER 3
ABSTRACT SECTION:
- What is the meaning of conventional treatment? Specify the type of treatment (exercise, exercise + nutrition, pharmacological, etc)
RESPONSE: Done
- Sample size calculation: see the protocols in the literature ((a sample size calculation was performed based on the medical histories of 80 adults presenting with oncologic pain))??
RESPONSE: There was an error with the translation since the sample calculation was made based on the antecedent, and the correction was made.
- When you refer “After the baseline assessment process,randomization, allocation concealment, and masking will be performed at different stages” which is the meaning of “different stages”. It refers to a different stages of the cancer or a different stages of the study period? Specify.
RESPONSE: The wording of this section was revised to generate clarity regarding the flow chart of the study.
- Limitations have not been included in the study by the authors, only strength points. Please. Add limitations of the study.
RESPONSE: Done
INTRODUCTION SECTION:
- At the end of the introduction, add the population and the main hypothesis: “Therefore, the present study aims to examine the effectiveness of PNE in relation to pain, biopsychosocial variables, and functional capacity compared with conventional management on X population”. The main hypotheses proposed are …
RESPONSE: Done
METHODS AND ANALYSIS SECTION:
- Very complete and adequate report.
RESPONSE: Thank you
DATA ANALYSIS SECTION:
- Declaration It is necessary to update to the 2020 CONSORT Declaration versión
RESPONSE: Done and updated the reference in materials and methods.

VERSION 2 – REVIEW

REVIEWER	Salazar-Méndez , Joaquín Universidad Santo Tomás, Escuela de Kinesiología, Facultad de Salud
REVIEW RETURNED	05-Apr-2023

GENERAL COMMENTS	Because the introduction was almost completely restructured, I send my suggestions to what was sent in this instance regarding this section. In general, the information that indicate is pertinent and is observed in a better way to understand the relevance of the investigation. However, you might prefer slight modifications. 1.-After “In addition, it is closely related to the decrease in quality of life and the increase in self-perceived disability” (second paragraph of the introduction) I could add some of the biopsychosocial variables that you will evaluate. This would give more meaning to considering these variables in your study and would generate a first approximation of the relevance of including them. 2.- in the third paragraph of the introduction, “Pain is one of the most feared and annoying symptoms among these patients (2,7). Another study reported that 5%–10% of cancer survivors have

	severe chronic pain that significantly impairs their function (8)" the use of the word "another" indicates a summative connector, so there must be a better wording to connect it with the previous sentence, since it is said that it is one of the most feared symptoms, but after speaking of percentages of chronic pain. 3.- The fourth paragraph generates a very abrupt change in the idea with respect to the previous paragraph. I suggest considering starting with some sentence that allows continuity with paragraph three, for example: "to avoid or control the adverse effects mentioned above, the relevant literature in oncology…" In the Outcomes section you indicate: "In particular, an assessment at baseline and 10 weeks after the intervention is considered." This can be understood as that the second evaluation will be carried out 10 weeks after the conclusion of the sessions due to the use of the word "after". I suggest indicating: "In particular, at baseline and at week 10 of the intervention the assessments will be carried out (or immediately post-intervention)". I understand that it is included in the supplementary material, which is pertinent, but it may be relevant to indicate it in the manuscript immediately to avoid confusion for those who do not have access to the supplementary material.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Dr. Joaquín Salazar-Méndez , Universidad Santo Tomás

Comments to the Author:

Because the introduction was almost completely restructured, I send my suggestions to what was sent in this instance regarding this section. In general, the information that indicate is pertinent and is observed in a better way to understand the relevance of the investigation. However, you might prefer slight modifications.

1.-After "In addition, it is closely related to the decrease in quality of life and the increase in self-perceived disability" (second paragraph of the introduction) I could add some of the biopsychosocial variables that you will evaluate. This would give more meaning to considering these variables in your study and would generate a first approximation of the relevance of including them.

Response: Done

2.- in the third paragraph of the introduction, "Pain is one of the most feared and annoying symptoms among these patients (2,7). Another study reported that 5%–10% of cancer survivors have severe chronic pain that significantly impairs their function (8)" the use of the word "another" indicates a summative connector, so there must be a better wording to connect it with the previous sentence, since it is said that it is one of the most feared symptoms, but after speaking of percentages of chronic pain.

Response: Done

3.- The fourth paragraph generates a very abrupt change in the idea with respect to the previous paragraph. I suggest considering starting with some sentence that allows continuity with paragraph three, for example: “to avoid or control the adverse effects mentioned above, the relevant literature in oncology…”

Response: Done

In the Outcomes section you indicate: “In particular, an assessment at baseline and 10 weeks after the intervention is considered.” This can be understood as that the second evaluation will be carried out 10 weeks after the conclusion of the sessions due to the use of the word “after”. I suggest indicating: “In particular, at baseline and at week 10 of the intervention the assessments will be carried out (or immediately post-intervention)”. I understand that it is included in the supplementary material, which is pertinent, but it may be relevant to indicate it in the manuscript immediately to avoid confusion for those who do not have access to the supplementary material.

Response: Done

We appreciate the recommendations.

VERSION 3 – REVIEW

REVIEWER	Salazar-Méndez , Joaquín Universidad Santo Tomás, Escuela de Kinesiología, Facultad de Salud
REVIEW RETURNED	15-Aug-2023

GENERAL COMMENTS	Congratulations on the work you have completed. The research you propose holds significant clinical relevance in an area that has been relatively underexplored. The protocol is highly suitable for publication.

VERSION 3 – AUTHOR RESPONSE

We appreciate the suggestions and recommendations. The suggested word change is generated, as is the inclusion of the approval of the committees in the summary. In the main text, they were already described, as were the number of minutes and date.
We remain attentive to any additional comments.

Editor(s)' Comments to Author (if any):
Please rename the "Ethics and Diffusion" section in the main text "Ethics and Dissemination".

Response: Done

- Please name all the ethics committees that has approved the study in the Ethics and Dissemination section in the Abstract and the main text.
Response: The information from the committees is included in the abstract; it was already included in the main text, and it is highlighted for better verification.

Comments to the Author:
Congratulations on the work you have completed. The research you propose holds significant clinical relevance in an area that has been relatively underexplored. The protocol is highly suitable for publication.
Response: Thank you.