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Manuscript: **“Bone Tissue Changes In The Background Of "Activation Of The Immune System" During Orthodontic Treatment And Tskaltubo Water Hormesis”**

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Peer review:

Reviewer 1: Irinel Panainte

Reviewer 2: Salome Omiadze, European University, Georgia

Reviewer 3: Jose Francisco Grillo, Egas Moniz Cooperativa de Ensino Superior-Portugal

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Questions	***Rating Result*** [Poor] **1-5** [Excellent]
1. The title is clear and it is adequate to the content of the article.	**5**
The title it is clear and adequate I agree with the content of the article	

2. The abstract clearly presents objects, methods and results.	**5**
The methods used are modern with relevant research, Methods and results are clearly presented and explained in the abstract and this is clearly shown in the abstract	
3. There are few grammatical errors and spelling mistakes in this article.	**4,5**
There is a slight grammatical error in the text that may not be considered a mistake, The text is simple and clear, which makes the article even better to read.	
4. The study methods are explained clearly.	**5**
The methods are quite well explained, The methods used are modern with relevant research,	
5. The results are clear and do not contain errors.	**5**
The results are good and reflect the relevance and scientific value of the topic	
6. The conclusions or summary are accurate and supported by the content.	**4**
The conclusions are accurately reflected and consistent with the text, it is extensive and exhaustive, but it can be said that it could have been written even shorter	
7. The references are comprehensive and appropriate.	**5**
The guidelines include something new that is perfectly modern as well as an article and hence the topic is also new and good	

Overall Recommendation (mark an X with your recommendation)：

Accepted, no revision needed	**X**
Accepted, minor revision needed	
Return for major revision and resubmission	
Reject	

Comments and Suggestions to the Author(s):

The article is written in good English, uses the latest methods, and references. The topic is a novelty in pilot dentistry and most importantly it grows bone tissue quite fast and it is important that you introduce new methods in dentistry.

Comments and Suggestions to the Editors Only:

I am thankful that I read this article in dentistry this part is very important in bone tissue regeneration and this modern hormesis method is quite well conveyed here and that this method has not negative effects.

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Reviewer Name: José Grillo Evangelista	
University/Country: Egas Moniz Cooperativa de Ensino Superior- Portugal	
Date Manuscript Received: 05-01-2022	Date Review Report Submitted:
Manuscript Title: Bone tissue changes in the background of "activation of the immune system" during orthodontic treatment and Tskaltubo water hormesis.	

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Questions	***Rating Result*** [Poor] **1-5** [Excellent]
1. The title is clear and it is adequate to the content of the article.	**4**
No comments	
2. The abstract clearly presents objects, methods and results.	**2**
The abstract does not clearly present the objectives, methods and results, it only mentions that an algorithm was developed but does not explain how. Does not show results	
3. There are few grammatical errors and spelling mistakes in this article.	**3**
Introduction **Line 3-** Osteoblasts are called large basophilic cytoplasmic cells that have the ability to synthesize protein- it's better- The osteoblasts are called large basophilic cytoplasmic cells that have the ability to synthesize protein **Line** 6- Cytokines secreted by mononuclear cells are chemical mediators that can interact directly or- It's better- The cytokines secreted by mononuclear cells are chemical mediators that can interact directly or **Line** 10- Prostaglandins stimulate bone resorption and increase the speed of orthodontic tooth movement- It's better- The prostaglandins stimulate bone resorption and increase the speed of orthodontic tooth movement. **Line** 13- transform into osteoblasts. Fibroblasts also migrate along the cement line and secrete thin- It'better- transform into osteoblasts. The fibroblasts also migrate along the cement line and secrete thin **Line** 29- This method is of practical importance because orthodontic treatment requires intensive- It's better- This method is of practical importance because the orthodontic treatment requires intensive **Line** 30- expensive medical services, treatment and, most importantly, time. Because patients have an- It's better- expensive medical services, treatment and, most importantly, time, because patients have an **Line** 40- characteristics play a very important role in orthodontic treatment. Radon therapy enables us to-It's better- characteristics play a very important role in	

orthodontic treatment. The radon therapy enables us to

Methodology

Line 1- Treatment was performed in two groups of patients (75 people), clinical and- It's better- The treatment was performed in two groups of patients (75 people), clinical and

Line 8- with boiled water at room temperature. None of the patients in the study had somatic disease, nor- It's better- with boiled water at room temperature. None of the patients in the study had somatic disease, or

Line 11- Quantitative lysozyme content in the oral cavity was determined by immunoenzymatic analysis- It's better- The quantitative lysozyme content in the oral cavity was determined by immunoenzymatic analysis

Line 15- Lysozym ELISA was also detected by IgA, IgG and IgM in venous blood by immunoenzymatic- It's better- The lysozym ELISA was also detected by IgA, IgG and IgM in venous blood by immunoenzymatic

Research data and discussion

Line 1- Patients were divided by sex as we did not establish a statistically significant difference between- It's better- The patients were divided by sex as we did not establish a statistically significant difference between

Line 10- treatment was administered. As can be seen from Table 1, there isa reliable difference between- It's better- 10treatment was administered. As can be seen from Table 1, there is a reliable difference between

Line 20- IgM) in venous blood differed significantly from the initial examination data ($p < 0.05$). Decreases- It's better- IgM) in venous blood differed significantly from the initial examination data ($p < 0.05$). The decreases

Line 35- Antibodies remained in both groups, moreover, in group 2 sIgA venous blood had statistically- It's better- The antibodies remained in both groups, moreover, in group 2 sIgA venous blood had statistically

Line 36- significant differences compared to the first group. ($p < 0.05$) (see Table 1, Figure 1). There was a- It´s better - It makes more sense the figure to be after its reference than to be where it is and the figure caption must be below and not above.

Line 40- IgA concentrations in the venous blood of all subjects corresponded to reliable values, although- It's better- The IgA concentrations in the venous blood of all subjects corresponded to reliable values, although

Line 65- suppressed, anti-inflammatory, desensitizing, and sedative action on tumor cells.It regulates the- t´s better- suppressed, anti-inflammatory, desensitizing, and

sedative action on tumor cells. It regulates the

Line 67- autoimmune and activates the action of nonspecific immune systems.All of the above allows us to- It's better- - autoimmune and activates the action of nonspecific immune systems. All of the above allows us to

Line 80- IL-6 is produced by activated monocytes or macrophages, endothelial cells, fibroblasts,- It's better- The IL-6 is produced by activated monocytes or macrophages, endothelial cells, fibroblasts,

4. The study methods are explained clearly.	**4**
No comments	
5. The results are clear and do not contain errors.	**2**

Figure 2: The movement of the bones and the formation of free spaces- It is not referenced in the text, the caption must be below and not above

Figure 3: Regulation of osteoclasts and osteoblasts through Tskaltubo water- It is not referenced in the text, the caption must be below and not above

6. The conclusions or summary are accurate and supported by the content.	**3**

Fig. 3: Mineralization of bone tissue and the use of Tskaltubo radon-containing water at the expense of activating the vascular system- It's better- **Fig.4** : Mineralization of bone tissue and the use of Tskaltubo radon-containing water at the expense of activating the vascular system- It is not referenced in the text, the caption must be below and not above

7. The references are comprehensive and appropriate.	**2**

References need to be reviewed.

2. ChandraA, Lin T. Tribble M. ZhuJ. Altman A.Tseng W. Zhang Y. et al .(2014). PTH1-34 alleviates radiotherapy-induced local bone loss by improving osteoblast and osteocyte survival. Bone 67, 33–40. It's better - ChandraA, Lin T. Tribble M. ZhuJ. Altman A. Tseng W. Zhang Y. et al. (2014). PTH1-34 alleviates radiotherapy-induced local bone loss by improving osteoblast and osteocyte survival. Bone 67, 33–40.

4. Choy M. WongR. Chow S. Li M. ChimY. Ho W. Cheng J. Cheung W. et al .(2020). How much do we know about the role of osteocytes in different phases of fracture healing? A systematic review. J. Orthop. Translat., 21, 111–121. It' better- Choy M. WongR. Chow S. Li M. ChimY. Ho W. Cheng J. Cheung W. et al. (2020). How much do we know about the role of osteocytes in different phases

of fracture healing? A systematic review. J. Orthop. Translat., 21, 111–121.

5. Donaubauer A. Deloch L. I Becker na, Rainer F., Benjamin F. and Udo S. .(2020). The Influence of Radiation on Bone and Bone Cells—Differential Effects on Osteoclasts and Osteoblasts International J. of Molecular Sciences. It's better- Donaubauer A. Deloch L. I Becker na, Rainer F., Benjamin F. and Udo S. (2020). The Influence of Radiation on Bone and Bone Cells—Differential Effects on Osteoclasts and Osteoblasts International J. of Molecular Sciences

Overall Recommendation (mark an X with your recommendation) ：

Comments and Suggestions to the Author(s):