RESPONSE TO REVIEWER

ESPS Manuscript NO: 14660

Dear Editor!

Thank you for your positive and encouraging feedback and the possibility to revise our manuscript. We hope that the revised version and the point by point response to the reviewers comments will enable our paper for publication in your renowned journal.

Reviewer#1 (00722438)

The Authors describe a valuable study which is well conducted and gives important clinical conclusions which may influence surgical and ethical conduct of interested surgical specialties. It is limited to the upper arm, short (20 min) time compression and the limited number of included volunteers. Authors gives reasonable answer to all these items. My final opinion is to accept for publication with the Journal.

Dear reviewer #2! Thank you for your positive feed back and your opinion to accept for publication.

Reviewer #2 (02444860)

Well designed and written paper, worth considering for publication.

Dear reviewer #3!

Thank you for your short but encouraging answer.

Reviewer #3 (02705067)

Although it is a well written and interesting manuscript the basic limitation is the time that the tourniquet applied or inflated. It was only for some minutes. The mane problem into the surgical operations is that the tourniquet is applied for some hours. The max is 2 hours and in long-lasting operations the tourniquet then is opened for 15 minutes and can be then inflated again. The problems are not only the local pressure and the vessels and nerves traumatic palses, but the release of secondary ischemia factors. It will better to inflate or apply tourniquet for 15-20 minuts at least.

Apart of that is a well written paper without any statistical problems and up-to-date. Please add a paragraph in discussion session for the time of tourniquet applied and the secondary ischemia factors be released (toxic for the cells in long-lasting operations).

Dear reviewer#4! Thank you for your positive feedback and mentioning the challenge with inflation time. We hope that the point by point response and the revised version of our paper will find your approval for publication.

1.Although it is a well written and interesting manuscript the basic limitation is the time that the tourniquet applied or inflated. It was only for some minutes. The mane problem into the surgical operations is that the tourniquet is applied for some hours. The max is 2 hours and in long-lasting operations the tourniquet then is opened for 15 minutes and can be then inflated again.

You are absolutely right that the inflation time of 20 minutes is not representing a setting in every days clinical practice. The problem why we were limited to that relatively short time, were regulations and restrictions by IRB and insurance company. In addition a tourniquet time of over 30 minutes without any local anesthesia is very painful as I know from self-experiments during preparation for the current paper. So we were limited to the 20 minutes, a time frame acceptable for study participants, but also for regulatory boards. We are planning a follow up project to solve that problem, based on the current publication.

2.The problems are not only the local pressure and the vessels and nerves traumatic palses, but the release of secondary ischemia factors. It will better to inflate or apply tourniquet for 15-20 minuts at least.

We totally agree to that statement, that is also in accordance to an already published paper by Karakoyun et al. in Eur J Vasc Endovasc Surg. They are stating that repeated short ischemic stimuli may reduce critical ischemic injury by promoting angiogenesis. This finding can be seen as a positive argument using the pneumatic tourniquet, were inflation and deflation can be performed every 60 minutes without big problems. By not discussing the release of ischemic factors during ischemia we were not deliberately ignoring that important fact, but wanted to focus on our investigated parameters and the produced results, in a paper with limited word count.

3.Apart of that is a well written paper without any statistical problems and up-to-date. Please add a paragraph in discussion session for the time of tourniquet applied and the secondary ischemia factors be released (toxic for the cells in long-lasting operations).

Thank your for that encouraging statement and acknowledgement of the proper work we have done.

The issue related to the tourniquet time was already included in the 1st version “Discussion, Limitations of the study”, 256-258. Due to your suggestion we will strengthen that message with a reference to clinical settings.
The challenge with “ischemic factors” is best fitted into limitations too, due to the fact that we did not investigated anything in this direction. We agree as stated previous, that this can be seen as a limitation, and therefore should be mentioned.

Reviewer#4 (02705621)

This is a research paper that compared a silicon ring and a pneumatic tourniquet in terms of their adverse effects. It seems that the topic of this paper seems to be important for the Orthopaedic surgeons. However, there are several points need to be clarified. 1. Abstract, line 39 to 40: The description of two “groups” is very confusing. In the abstract, the authors said “group A” used a silicon sling and “group B” used pneumatic tourniquet. However, all the subjects were actually examined with both devices. Please reword. 2. Abstract, line 44 to 49: No data were shown in the abstract. Please indicate the data of pain scores. 3. Line 79: InternationalConference: Please insert a space between two words. 4. Line 119: T2-TSE(turbo…: Please insert a space between two words. 5. Line 133 to 145: In this part, the authors wrote that the standard pneumatic tourniquet was used in Group A, and the HemaClear was used in Group B, respectively. Were these correct? Moreover, please consider rewording since all the subjects were investigated with both devices. 6. Line 151: following parameters were evaluated: blood pressure, were VAS… Please delete later “were”. 7. Line 157: Is “sequenzes” mistyped? 8. Line 175 to 184: No data was shown for the MRI measurements. Although the authors did not find any significant differences, they should present the results of the measurements at least in the Results section. 9. Line 189 to 199: The data presentation concerning both VAS and FPS levels were confusing. Although both VAS and FPS were significantly lower in Group A than those in Group B, the authors said that Hemaclear was more painful. Please explain. 10. Line 191 to 193: “VAS and FPS levels, post removal, were 1 / 1 in only two volunteers, both male and occurring after Day1 with the HemaClearTM device.” What is 1/1? Please reword this sentence. 11. Line 196 to 199: “VAS and FPS levels, post removal, were 1 / 1 in only two volunteers, both male and occurring after Day1 with the HemaClearTM device.” This sentence should be moved in the discussion. 12. Line 218 to 220: “The substituted opinion by McEwen and his study group is in sharp contrast to findings of other various trials, and may be influenced by commercial interests ?1,2,4,13-16?. “ The description in this sentence is not clear. What is “commercial interests”? Please explain clearly. 13. Line 235 and 236: “sheer force” Is this “shear force”? If so, please

explain more clearly the pathomechanism that the pneumatic tourniquet causes the "shear force" during surgery without any active motions. 14. Line 361 to 364: Neither Tab. 1 nor Tab.2 was included in the manuscript. Moreover, they were not explained in the text. 15. Fig. 2a and 2b: The neurovascular bundles were too small to identify in each picture. Please resubmit figures with higher magnification.

Dear reviewer#1! Thank your for your extensive but controversial comments regarding our paper. We honor the fact that you suggest our paper for major revision, even if you have some major concerns, as stated in your comments. After careful considerations with the involving authors we provided the point by point response and the changes in the revised paper, where suitable. We are well aware that not all of your suggestions are implemented in the revised version, a fact that is also based on other reviewers judgment. Despite that regrettable circumstance we hope that a publication of the paper in it´s revised version is a possible proceeding for you.

This is a research paper that compared a silicon ring and a pneumatic tourniquet in terms of their adverse effects. It seems that the topic of this paper seems to be important for the Orthopaedic surgeons. However, there are several points need to be clarified.

Thank your for understanding the message of our paper and the actuality of the topic.

1. Abstract, line 39 to 40: The description of two "groups" is very confusing. In the abstract, the authors said "group A" used a silicon sling and "group B" used pneumatic tourniquet. However, all the subjects were actually examined with both devices. Please reword.

We can retrace the thought that lead to your suggestion, but we cannot agree to that after careful consideration. The term "group" is clearly related to the different devices, and not as suggested by you, to different groups of volunteers. Also in the "Results" section it is clearly stated " …we were able to acquire data from 14 placements of each device." Therefore we included "variantly" between "placement" and "on" to meet your concerns in the best possible way.

2. Abstract, line 44 to 49: No data were shown in the abstract. Please indicate the data of pain scores.

We agree that providing the data might improve the impact of the abstract, and therefore data for pain scores are now included in the revised version.

3. Line 79: InternationalConference: Please insert a space between two words.
Correction was performed according to your suggestion.

4. Line 119: T2-TSE(turbo…: Please insert a space between two words.
Correction was performed according to your suggestion.

5. Line 133 to 145: In this part, the authors wrote that the standard pneumatic tourniquet was used in Group A, and the HemaClear was used in Group B, respectively. Were these correct? Moreover, please consider rewording since all the subjects were investigated with both devices.

We apologize for that incoherence according to group labeling in the first version of our paper. In the revised version we checked the entire manuscript for consistent labeling. As stated under 1. , we are unable to follow this suggestion.

6. Line 151: following parameters were evaluated: blood pressure, were VAS… Please delete later "were".

Correction was performed according to your suggestion.

7. Line 157: Is "sequenzes" mistyped?

Sorry for that typing error, correction was performed according to your suggestion.

8. Line 175 to 184: No data was shown for the MRI measurements. Although the authors did not find any significant differences, they should present the results of the measurements at least in the Results section.

We can understand your demand for data, but in our opinion it does not make any sense to present all individual measurements, resulting in several tables with a lot of digits leading to nowhere. This is confusing for the reader, and therefore we used the included figures and table to demonstrate the equality in both groups.

9. Line 189 to 199: The data presentation concerning both VAS and FPS levels were confusing. Although both VAS and FPS were significantly lower in Group A than those in Group B, the authors said that Hemaclear was more painful. Please explain.

As detected by you in 5. earlier, this is due some incoherent group labeling during writing the manuscript and cannot be seen as a scientific mistake. We carefully checked correct labeling of the two groups through out the entire revised version, to avoid confusion in the future.
Explanation why Hemaclear was described as more painful is stated in line 230-235 in the revised version.

10. Line 191 to 193: "VAS and FPS levels, post removal, were 1 / 1 in only two volunteers, both male and occurring after Day1 with the HemaClearTM device." What is 1/1? Please reword this sentence.

1 / 1 was replaced by 1 and 1, correction was performed according to your suggestion.

11. Line 196 to 199: "VAS and FPS levels, post removal, were 1 / 1 in only two volunteers, both male and occurring after Day1 with the HemaClearTM device." This sentence should be moved in the discussion.

Contrary to your intention, we think that this sentence, as it is a result, fits best under "Results" and not "Discussion". As the VAS and FPS scale goes from 0-10 and 0-5, no further discussion of that finding is in the readers interest.

12. Line 218 to 220: "The substituted opinion by McEwen and his study group is in sharp contrast to findings of other various trials, and may be influenced by commercial interests ?1,2,4,13-16?. " The description in this sentence is not clear. What is "commercial interests"? Please explain clearly.

After reading the introduction line 65-66 and the papers by McEwen et al., especially the one in JBJS by Noordin S. published in 2009, the answer should be quite clear. McEwen is the inventor of the technique that is behind the A.T.S. ®3000 Automatic Tourniquet System by Zimmer Inc.. With that knowledge, the answer for "commercial interests" is more than obvious. In their papers, they are blaming silicon ring similar devices as dangerous. I do not want to get into detail but in the past there were some actions that can be considered far

below the belt. At this point I want to make clear that I do not receive beneficiaries from either side.
In accordance with the co- authors I decided to mention that fact in a neutral and most polite and educated manner, because a discussion in a scientific paper is not a place where personal feelings or court like tendencies should be exchanged. By stating “may be influenced” and giving the citations for the related papers, every reader has the choice to build his own opinion on this matter.

13. Line 235 and 236: “sheer force” Is this “shear force”? If so, please explain more clearly the pathomechanism that the pneumatic tourniquet causes the “shear force" during surgery without any active motions.

Sorry for the typing error, it should mean “shear”. The mechanism leading to shear force is described in detail in lines 228 – 239, and in figure 3. Shear force is the result of pressure that takes affect on the surface, and has nothing to do with any movement. This is especially interesting at the edges of both devices. As you can see in figure 3, the maximum level of pressure is 60, compared to 90 in the pneumatic tourniquet. This is resulting in lesser shear forces on the soft tissue, caused by the pressure of the device in the silicon ring, compared to the pneumatic tourniquet. We hope that this issue is now clearly explained.

14. Line 361 to 364: Neither Tab. 1 nor Tab.2 was included in the manuscript. Moreover, they were not explained in the text.

We apologize for that error. There was obviously a problem of our side when it comes to the submission of the tables. Explanation in the text in the “Results” section and tables are included in the revised version.

15. Fig. 2a and 2b: The neurovascular bundles were too small to identify in each picture. Please resubmit figures with higher magnification.

We are sorry but a higher resolution for exporting is not possible, due to existing technical conditions. If we would enlarge the existing images any further, it would result in fuzzy white dots without any meaning. The reason for showing the images in figure 2a and 2b is not to give the reader the possibility to prove our measurements, they were performed by experienced physicians from Dep. Radiology on special high resolution screens, using a software developed only for that purpose, but to get an impression how the soft tissue conditions change after a relatively short time with compression.