Reviewer A

Comment: With interest I read the manuscript 'Three-dimensional computed tomography mapping and clinical predictive factors for the morphologic characterization of displaced femoral neck fractures.

Reply: Thank you for your support and valuable comments. We have revised our manuscript based on the suggestions.

Comment: As first comment I advise the authors to completely re-read the manuscript and check and adjust the Academic English.

Reply: Thank you for your kind reminder. We have re-read the manuscript, meanwhile, we revised it by checking and adjusting the Academic English, also according to all related suggestions.

Comments:

Comment 1: In the results section of the abstract, the second sentence ends with "...femoral neck and the only part." This sentence is not clear. Please rephrase.

Reply 1: Thank you for this constructive comment. "and the only part" seems redundant, and it has been deleted.

Changes in the text: We have modified our text as advised (see Page 1, line 22).

Comment 2: "related factors" is not a suitable keyword as this is too general.

Reply 2: Thank you for your kind reminder. Since our findings were related to age and fracture classification, "related factors" in the Keywords section have been replaced by "age" and "fracture classification".

Changes in the text: We have modified our text as advised (see Page 2, lines 14-15).

Comment 3: The definition of the different parts of the femur (for instance "2.5th to 4.5th (5th) part" is not clear. Please include an image in which this will be clarified.

Reply 3: We appreciate this valuable advice. Due to the unclear definition of the different parts of the femur (for instance "2.5th to 4.5th (5th) part"), it has been clarified in Figure 8.

Changes in the figure: We have modified our figure as advised (see Figure 8).

Comment 4: In the introduction it is mentioned that the incidence of femur fractures
increases with the aged population and traffic incidence. Next to a missing reference. the first is true, the second not. Please adjust.

Reply 4: Thank you for this constructive comment. Since the second one is not true, it has been deleted. Meanwhile, a related reference has been also added to this content

[Reference: Harvey, N C et al. “Impact of population-based or targeted BMD interventions on fracture incidence.” Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA vol. 32,10 (2021): 1973-1979].

Changes in the text: We have modified our text as advised (see Page 2, line 19).

Comment 5: Also in the introduction the authors mention: "However, clinical decision-making in hip surgery is still controversial." Why? Explain.

Reply 5: Thank you for your careful check and kind reminder. Because controversy regarding the choice of procedure exists mainly in the management of displaced femoral neck fractures, whether the fracture was displaced plays an important role in surgical decision-making [Reference: Jain, Nitin B et al. “Trends in surgical management of femoral neck fractures in the United States.” Clinical orthopaedics and related research vol. 466,12 (2008): 3116-22]. In addition, treatment of displaced femoral neck fractures includes internal fixation and arthroplasty. However, whether arthroplasty or internal fixation is the primary treatment for displaced femoral neck fractures in elderly patients remains a subject for debate [Reference: Gao, Hongwei et al. “Which is the best alternative for displaced femoral neck fractures in the elderly?: A meta-analysis.” Clinical orthopaedics and related research vol. 470,6 (2012): 1782-91]. "However, clinical decision-making in hip surgery is still controversial" is unclear, so we have changed it into "However, the best surgical management of displaced femoral neck fractures remains controversial" followed by the reference [Reference: Fischer, H et al. “Management of proximal femur fractures in the elderly: current concepts and treatment options.” European journal of medical research vol. 26,1 86].

Changes in the text: We have modified our text as advised (see Page 3, lines 1-2).

Comment 6: In the hypothesis (introduction) related factors are mentioned. Please explain what related factors are.

Reply 6: Thank you for the reminder. Age is used in many treatment algorithms for patients with displaced femoral neck fractures. In addition, fracture classifications were commonly used in the practice of femoral neck fractures [Reference: Heetveld, Martin J et al. “Femoral neck fractures: can physiologic status determine treatment choice?.” Clinical orthopaedics and related research vol. 461 (2007): 203-12 & Jain, Anil K et al. “Treatment of neglected femoral neck fracture.” Indian journal of
Hence, we hypothesized that bone defects were associated with age and fracture classifications. Also, "including age and fracture classifications" was added to explain related factors.

Changes in the text: We have modified our text as advised (see Page 3, lines 20-21).

Comment 7: The ethics statement is missing in the materials and methods section.
Reply 7: Thank you for your careful check. This study was approved by the Institutional Review Board of our institution. So, the ethics statement was added.
Changes in the text: We have added the ethics statement (see Page 4, line 4).

Comment 8: Please clarify the discrepancy in slice thickness of > 3mm (paragraph subjects) and 1.0 mm (radiological analysis).
Reply 8: Thank you for your constructive comments. The exclusion criteria of a slice thickness are referred to in the previous paper. The exclusion criteria of a slice thickness of > 3mm (Subjects) was firstly reported in the 3D mapping study [Reference: Xie, Xuetao et al. “Two and Three-Dimensional CT Mapping of Hoffa Fractures.” The Journal of bone and joint surgery. American volume vol. 99,21 (2017): 1866-1874]. Hence, we used this exclusion criterion of the slice thickness in the Subjects section. However, we obtained CT images with a slice thickness of 1.0 mm. So, we used "1.0 mm thick slices" in the Radiological Analysis section. In addition, the exclusion criteria of a slice thickness of > 1mm were also reported [Reference: Ye, Kai et al. “Intra-articular fragment mapping in associated both-column acetabular fractures.” Archives of orthopaedic and trauma surgery, 10.1007/s00402-022-04381-w]. To avoid misunderstanding, we have deleted "(1.0 mm thick slices)" in the Radiological Analysis section. And, we changed “the slice thickness of > 3mm” (Subjects) into “the slice thickness of > 1mm”.
Changes in the text: We have modified our text as advised (see Page 4, line 10 and line 18).

Comment 9: Explain why the mentioned exclusion criteria are chosen.
Reply 9: Thank you for your careful check. The exclusion criteria of a slice thickness referred to the previous 3D mapping study [Reference: Ye, Kai et al. “Intra-articular fragment mapping in associated both-column acetabular fractures.” Archives of orthopaedic and trauma surgery, 10.1007/s00402-022-04381-w]. The femoral neck fracture with femoral head fracture commonly occurs in a high-energy injury. The high-energy injury with femoral head fracture can affect the Virtual Reduction, so the process for bone defect generation would be influenced as well. However, no fracture combined with femoral head and neck was found in this study due to the rarity of femoral head fractures. The trauma mechanism for all included patients is not available in our maintained orthopedic database, so it is inappropriate to treat the
high-energy injury as an exclusion criterion in this study. We are sorry for the confusion, and we have deleted "high-energy injury". In addition, the two processes, Virtual Reduction & Bone Defect Generation, would also be affected by bilateral femoral neck fractures, and congenital or acquired malformation of the femoral neck. Bone destruction caused by pathologic fractures may affect the process of bone reconstruction and bone defect measurement. Also, the injury mechanism and treatment of Pathological fractures were different from the general fracture, so pathological fractures were excluded from this study. Hence, the mentioned exclusion criteria are chosen.

Changes in the text: We have deleted "high-energy injury" to avoid misunderstanding (see Page 4, line 10).

Comment 10: "Gender" is not a scientific term, please change to 'sex' (data analysis paragraph).
Reply 10: Thank you for your kind reminder. "Gender" (Statistical Analysis paragraph) has been changed into "sex".
Changes in the text: We have modified our text as advised (see Page 6, line 22).

Comment 11: In table 1, the sample group is divided between adults and elderly. Why has this been done? BMD? Also, a statistic analysis should be done to check for significant differences between both groups for all factors mentioned in table 1.
Reply 11: We appreciate this valuable advice. As the reviewer said, elderly patients will probably sustain most fractures due to a fall. In younger patients, more high-energetic traumas will be found. Also, age is an important consideration for the clinical assessment of patients with displaced femoral neck fractures. BMD may not be used in a routine examination when a femoral neck fracture is suspected. Hence, we divided the sample group into two groups, adults and the elderly, according to the WHO standard definition of the elderly. In addition, a statistical analysis has been done to check for significant differences between both groups for all factors mentioned in table 1. The statistics used also has been added to the Statistical Analysis section. The results also have been added to the Results section. The related content also was added to the Discussion section, and it was placed before the content of linear regression analyses in adult and elderly groups.
Changes in the manuscript: We have modified our table as advised (see Table 1). We have also added the statistics to our text as advised (see Page 6, lines 15-17). We have also added the results to our text as advised (see Page 7, lines 8-10). We have also added the results to the Discussion section in our text as advised (see Page 11, lines 7-8).

Comment 12: Has the trauma mechanism for all included patients been investigated?
Elderly patients will probably sustain most fractures due to a fall. In younger patients, more high-energetic traumas will be found.

Reply 12: Thank you for your constructive comments. Unfortunately, the trauma mechanism for all included patients is not available in our maintained orthopedic database. So the trauma mechanisms for all 256 patients were not included in this study.

Comment 13: In the linear regression analysis paragraph, table 2 is mentioned. The significance of the results is not presented in the table.
Reply 13: Thank you for your careful check. The significance of the results has been presented in table 2 by using the “*”. And, “**” Represents a related factor with statistical differences (P<0.05).
Changes in the table: We have modified our table as advised (see Table 2).

Comment 14: The fracture lines which are shown in the different images are not clearly visible. Please enhance the contrast of the images.
Reply 14: Sorry for the confusion. We have enhanced the contrast of the images regarding the fracture lines to make them visible.
Changes in the figure: We have modified our figures as advised (see Figures 4 and 5).

Comment 15: The figure captions always mention panel A, B, C and so on. However, in the images this I, II, III and IV is used. Please adjust this.
Reply 15: Sorry for the confusion. To maintain consistency, we have adjusted all related images by using A, B, C, and so on.
Changes in the figure: We have modified our figures as advised (see Figures 1, 2, 3, and 8).

Comment 16: Include a color legend in figures 1, 2 and 3.
Reply 16: Thank you for your constructive comments. We have respectively added a color legend to figures 1, 2, and 3.
Changes in the figure: We have modified our figures as advised (see Figures 1, 2, and 3).
Reviewer B

Comment: This manuscript presents a clinical data based study to characterize morphological factors that lead to displaced femoral neck fractures. In the opinion of the reviewer, this line of research is very important for the patient specific predictive diagnosis and surgical planning applications. The study is based on a large amount of clinical data that has been verified independently by two experts. The reviewer thinks that the manuscript could be a valuable scientific contribution.

Reply: We appreciate the reviewer’s high comments and support of our work.

The reviewer has minor editorial concerns that revolve around the following points: Comment 1: The citation labels in this paper are always after the full stop. For example, in the last line of the first paragraph of introduction “…..given to internal fixation. (2)” It should be “…..given to internal fixation (2).” Citation labels are part of the sentences. Please correct this throughout the manuscript.

Reply 1: Thank you for your careful check and kind reminder. Citation labels are part of the sentences, so we have corrected this throughout the manuscript.

Changes in the text: We have modified our text as advised (see All citation labels in the text).

Comment 2: In Figures 1, 2, 3, and 8, the subfigures labels in the figures are “I, II, III” while they are denoted as “a, b, c” in the captions. Please make them consistent.

Reply 2: Sorry for the confusion. To maintain consistency, we have adjusted all related images by using A, B, C, and so on.

Changes in the figure: We have modified our figure as advised (see Figures 1, 2, 3, and 8).

Comment 3: An introductory figure outlining the key anatomical features of femur bone would help the readers in understanding the important keywords used in the manuscript.

Reply 3: Thank you for your constructive comments. We agree that an introductory figure outlining the key anatomical features of femur bone would help the readers in understanding the important keywords used in the manuscript. So, we have respectively added a color legend to figures 1, 2, and 3 to describe the key anatomical features of the femur bone and help the readers understand the important keywords. In addition, the definition of the different parts of the femur (for instance "2.5th to 4.5th (5th) part") also has been clarified in Figure 8.

Changes in the figure: We have modified our figures as advised (see Figures 1, 2, 3, and 8).
Comment 4: The precise difference between fracture lines and bone defects are not clear. How bone defects are objectively measured?
Reply 4: Thank you for your careful check and kind reminder.
Our method used in the 3D mapping process in this study is the same as those used in previous literature [References: Zhan, Yu et al. “Three-dimensional fracture mapping of multi-fragmentary patella fractures (AO/OTA 34C3).” Annals of translational medicine vol. 9,17 (2021): 1364 & Li, Ruiyang et al. “Three-dimensional computed tomography mapping and analysis of distal femur fractures (AO/OTA types 33A, 33B, and 33C).” Annals of translational medicine vol. 10,7 (2022): 398]. In addition, the same method was used for the 3D mapping of the fracture lines and the bone defects. Therefore, the same method yields nearly identical precise.
The measurement of the bone defects is conducted as followings. After the fracture fragments were reconstructed, these fragments were visually reduced based on the contralateral femoral neck. Boolean operations were then used to obtain the model of the bone defect based on the contralateral femoral neck and the reduced fragments. The models of the bone defect and the fracture fragments were aligned and repositioned onto the template model. Finally, the area of bone defects was determined, when the bone defects were mapped on the surface of the template femoral neck (also see Figure 2). In this way, we could automate the generation of the area in the software so as to guarantee objectivity. In addition, an almost perfect inter- and intra-observer reliability for the bone defect mapping was demonstrated in this study.

Comment 5: The data sets are first segmented and then rendered for the visualization. A short summary on the segmentation methods would be helpful for the readers to understand the challenges and time cost of such studies. A few of the papers in this context are:
Zoroofi, R.A., Sato, Y., Sasama, T., Nishii, T., Sugano, N., Yonenobu, K., Yoshikawa, H., Ochi, T. and Tamura, S., 2003. Automated segmentation of acetabulum and femoral head from 3-D CT images. IEEE Transactions on Information Technology in Biomedicine, 7(4), pp.329-343.
Krčah, M., Székely, G. and Blanc, R., 2011, March. Fully automatic and fast segmentation of the femur bone from 3D-CT images with no shape prior. In 2011 IEEE international symposium on biomedical imaging: from nano to macro (pp. 2087-2090).IEEE.
Gangwar, T., Calder, J., Takahashi, T., Bechtold, J.E. and Schillinger, D., 2018. Robust variational segmentation of 3D bone CT data with thin cartilage interfaces. Medical Image Analysis, 47, pp.95-110.
Reply 5: Thank you for your thoughtful and helpful comments on our manuscript. The 3-matic software was widely used in the 3D mapping studies, and the process of the 3D mapping has been described and acknowledged [References: Zhan, Yu et al. “Three-dimensional fracture mapping of multi-fragmentary patella fractures (AO/OTA 34C3).” Annals of translational medicine vol. 9,17 (2021): 1364; Li, Ruiyang et al. “Three-dimensional computed tomography mapping and analysis of distal femur fractures (AO/OTA types 33A, 33B, and 33C).” Annals of translational medicine vol. 10,7 (2022): 398; Xie, Xuetao et al. “Two and Three-Dimensional CT Mapping of Hoffa Fractures.” The Journal of bone and joint surgery. American volume vol. 99,21 (2017): 1866-1874]. The segmentation is one of the important steps in the 3D reconstruction of the displaced femoral neck fracture, and the raw CT data sets are first segmented in the 3-matic software. Then DFNF fragments were multiplanar reconstructed in Mimics and virtually reduced, with the contralateral proximal femur as a standard, in the 3-matic software. In addition, the segmentation is a function of the 3-matic software. The principle of the segmentation method in software may be similar to that in the three papers recommended. To improve the understanding of the challenges and time cost of this studies, we have added the content of the segmentation to the text with references recommended [References: Zoroofi, R.A., Sato, Y., Sasama, T., Nishii, T., Sugano, N., Yonenobu, K., Yoshikawa, H., Ochi, T. and Tamura, S., 2003. Automated segmentation of acetabulum and femoral head from 3-D CT images. IEEE Transactions on Information Technology in Biomedicine, 7(4), pp.329-343; Krčah, M., Székely, G. and Blanc, R., 2011, March. Fully automatic and fast segmentation of the femur bone from 3D-CT images with no shape prior. In 2011 IEEE international symposium on biomedical imaging: from nano to macro (pp. 2087-2090).IEEE & Gangwar, T., Calder, J., Takahashi, T., Bechtold, J.E. and Schillinger, D., 2018. Robust variational segmentation of 3D bone CT data with thin cartilage interfaces. Medical Image Analysis, 47, pp.95-110]]. Changes in the text: We have modified our text as advised (see Page 4, lines 19-21 and Page 5, lines 2-3).

Comment: Additionally, the reviewer suggests to open source the data. This dataset contains significant clinical data that has been segmented and validated for fracture lines and bone defects by medical experts. This dataset can be much helpful to the broader scientific community that is interested in the image analysis of bone, bone mechanics, and bone-disease diagnosis. In return, this work will reach to much wider audience.

Reply: We thank the reviewer very much for the high evaluation and kind recommendation. We are happy to share raw data/patient information related to the article with the broader scientific community (see Data Sharing Statement attached).
Comment: In summary, the reviewer thinks that the manuscript could be a valuable contribution to this journal. Given the above critical points, the manuscript requires a “minor review.”

Reply: Thank you for your support and valuable comments. We have revised our manuscript in line with the suggestions.