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March 31, 2017
World Journal of Orthopedics
Science Editor, Editorial Office
Fang-Fang Ji,

Dear Fang-Fang

RE: Manuscript ID: 32558 | Sakamoto et al.

As the corresponding author, and on behalf of my coauthors, I would like to thank you for considering our case series article titled “Non-ossifying fibromas: Case series, including in uncommon upper extremity sites” for publication in *World Journal of Orthopedics.*
We are grateful for the time and effort spent by the journal and external reviewers to review our manuscript and provide knowledgeable feedback that strengthens our paper.

We hope that you will now find the revised manuscript suitable for publication and we extend our appreciation once more for the opportunity to have our manuscript under review at *World Journal of Orthopedics.*
Sincerely yours,

Akio Sakamoto, M.D., Ph.D.

1 What did this study explore?

Non-ossifying fibromas are common benign fibrous lesions in the lower extremities of children. The lesions are less common in the upper extremities. Non-ossifying fibromas are considered to be a developmental bone defect rather than a true neoplasm. However, the histology of non-ossifying fibromas is identical to that of benign fibrous histiocytoma, which is a neoplastic lesion. We wanted to distinguish the clinical characteristics of non-ossifying fibromas from the aggressiveness of neoplastic lesions. We also wanted to clarify the anatomical differences between the common sites of the lower extremities and the less common site of the upper extremities.

2 How did the authors perform all experiments?

Non-ossifying fibromas are thought to be a developmental bone defect. Small non-ossifying fibromas have no clinical significance. Therefore, we collected the non-ossifying fibroma cases which were referred with a working diagnosis of neoplastic lesions. Consequently, large non-ossifying fibromas with possible aggressive characteristics, as well as non-ossifying fibromas in rare locations, were collected. Clinical information and plain radiographs were analyzed for these cases.

3 How did the authors process all experimental data?

We analyzed 44 cases of non-ossifying fibromas including 47 lesions comprising two upper extremity cases and 45 lower extremitiy cases. Clinical information and findings from plain radiographs were collected. The findings associated with possible aggressiveness, such as incidence of fracture and radiographic findings related to size and expansiveness, were further analyzed.

4 How did the authors deal with the pre-study hypothesis?

Larger lesions >4 cm and lesion expansion at the cortex were seen in 21% and 32% of non-ossifying fibroma cases, respectively. Two patients suffered from fracture and were

treated without surgery, one in the radius and one in the femur. Non-ossifying fibromas in the lower extremity had fewer clinical problems, regardless of their size and expansiveness. On the other hand, lesions in the upper extremities in the humerus and the radius were expansive at the cortex, and lesion size increased with slow ossification, suggestive of aggressive biological features. It seems that there is a site specific difference, especially between the upper extremity and the lower extremity.

5 What are the novel findings of this study?

There is a site specific difference, especially between the upper extremity and the lower extremity. Non-ossifying fibromas in the lower extremity are considered to be a developmental bone defect rather than a true neoplasm, even those that are large and expansive. Lesions in the humerus and the radius were expansive at the cortex and lesion size increased with slow ossification. Furthermore, non-ossifying fibromas in the radius are predisposed to fracture because of the slender structure of the radius and the susceptibility to stress.