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研究題目：う蝕・歯周疾患の予防を目指した若年者矯正歯科治療に伴って生じうる根尖部歯根吸収機構解明と予防への取り組み

目　的：

External apical root resorption（EARR）is an irreversible clinical complication secondary to orthodontic treatment resulting in shortening of root length. It is a critical problem that is very difficult to prevent or predict. To better prevent this complication, lots of researchers have attempted to clarify the precise cellular mechanism concerning EARR. But it is still not fully understood. In order to provide mechanisms and prevention for EARR, this research is going to investigate how some of the essential cytokines concerning EARR will change over time during this process and the possibility of preventing EARR.

対象および方法：

Sprague-Dawley rats（Japan SLC, Shizuoka, Japan）were used for all experiments. The rats were housed in separate cages in a 12-h light / dark environment at the constant temperature. Continuous mechanical light force of 3cN was applied to the first molar（M1）of the rats in the mesio-distal direction by Nickel-titanium alloy round wires of 0.15-mm diameter and 12-mm length（Furukawa Electric Co. Ltd., Tokyo, Japan）to induce orthodontic tooth movement（OTM）. The left side of the rats were used as force application（FA）group and the right side was used as control group. The rats were euthanized after 0.25 days, 0.5 days, 1 day, 3 days, 5 days, 7 days, 10 days and 14 days of tooth movement（n＝6 each ）, the maxillae were harvested immediately and fixed in 4% paraformaldehyde/PBS for 48 hours in 4° C.

First of all, the radiological assessment were applied to the sections. The maxillae were scanned using a micro-focus X-ray computed tomography system（SMX-100CT；Shimadzu, Kyoto, Japan）for all groups. The micro-CT conditions were set at 90 kV, 100 mA, and a 10-mm field of view. Image data of the maxillary first molars were reconstructed using an image analysis software package（TRI/3D-BON；Ratoc System Engineering, Tokyo, Japan）. OTM distance was measured by Image J software（Image J；National Institutes of Health, Bethesda, MD, USA）. The distance from the distal surface of the maxillary M1 to the mesial surface of the maxillary second molar（M2）was measured as the amount of OTM. In the reconstruction images, root volume was analyzed. The root starts from dento-enamel junction to apex were selected as the part of root volume to be measured. Reconstruction of 3-Dimension structure of the root was established and measured by TRI/3D-BON. Then the histological assessment was applied to the section. After fixation, the maxillae were decalcified

in 10% EDTA（pH 7）for 5 weeks at 4℃. The tissue blocks were then embedded in paraffin, and 4-μm-thick serial sagittal sections of the first molar region were made and subjected to hematoxylin and eosin（H-E）staining, Tartrate resistant acid phosphatase（TRAP）staining. The morphology and resorption condition of each group were observed by H-E staining. To confirm odontoclastgensis, the sections were stained with TRAP solution, then counterstained with hematoxylin. Immunohistochemistry for sclerostin were conducted to figure out whether and how sclerostin would interact with other important factors, influence EARR.

結果および考察：

Body weight was measured every day after force application. There is a decrease of the body weight immediately after 1 day of force application. But it returned to normal condition and start to increase again after 3 day of force application. Tooth movement distance was measured using micro-CT image. The tooth movement distance showed there is an immediate increase of tooth movement distance after 1 day of force application. But the tooth stopped moving until the fifth day of force application.（Fig.1）

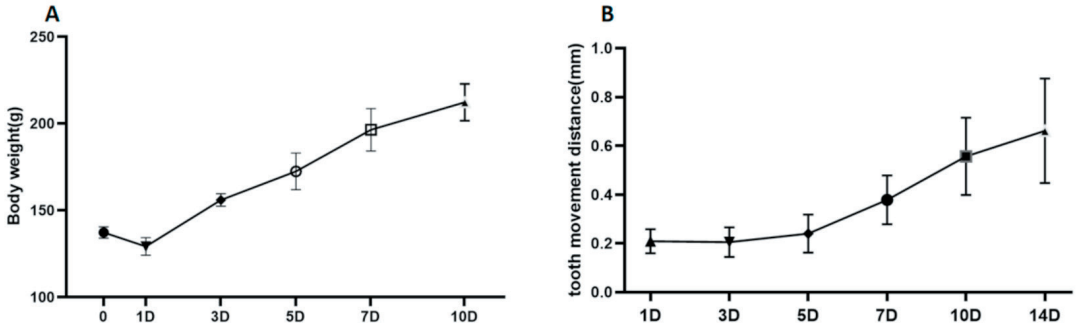

Fig.1 Characterization of tooth movement in M1.（A）The change of body weight of SD rats after tooth movement.（B）Quantification of tooth movement distance after force application.

The immediate tooth movement might originate from the compression of periodontal ligament（PDL）. On the fifth day of force application hyalinization and apical root resorption could be observed from H-E staining and TRAP staining.（Fig.2）According to the former research, the compression of PDL will lead to the compression of blood vessel inside PDL which will farther induce the hypoxia status inside PDL and cause inflammation. The inflammatory factors and cytokines will lead to bone resorption and apical root resorption. Sclerostin, which is encoded by the SOST gene and predominantly secreted by mature osteocytes and cementocytes, was discovered to be an antagonist of the canonical WNT pathway. Sclerostin is also considered as one of the most important inflammatory factors leading to the maturation of osteocytes and bone resorption. But the relationship between sclerostin and apical root resorption remains unclear. Immunohistochemistry staining of sclerostin was conducted, the result showed that sclerostin decreased gradually after 3 days of

force application on distal side of the root. While on mesial side of the root inside compressed PDL the expression remains the same as compared with control group. On 5 days of tooth movement the expression of sclerostin almost disappeared after apical root resorption appeared. This result demonstrated that sclerostin related to the bone resorption on mesial side of the root while on distal side where apical root resorption appeared the inhibition of the expression of sclerostin occurred. The possible explanation is that the bone formation process inhibits the expression of sclerostin or the activity of cementocytes which express sclerostin is suppressed. Farther research should be conducted to provide better understanding of apical root resorption in the further.

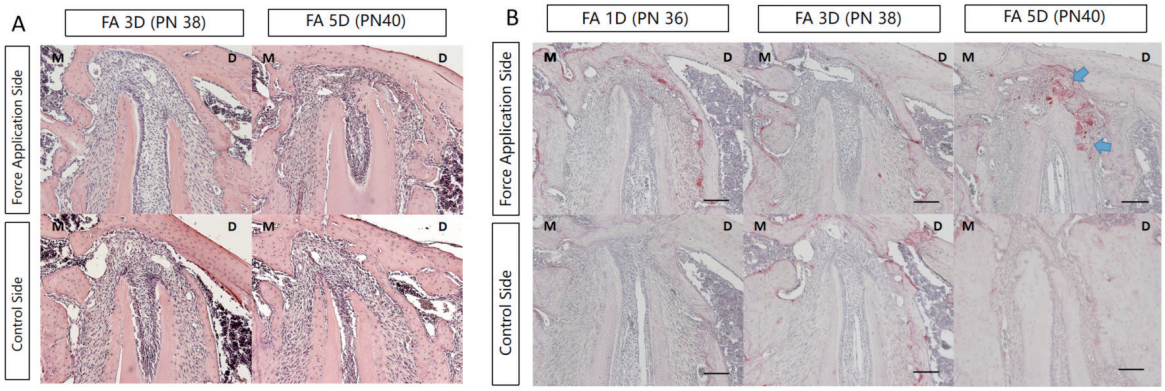

Fig.2 Histological assessment of root after OTM.（A）Image of H-E staining in both control group and force application group after 7 days of OTM.（B）Compression force induces odontoclastgensis during OTM. Image of TRAP staining after tooth movement in control group and force application group. M, mesial side；D. distal side.

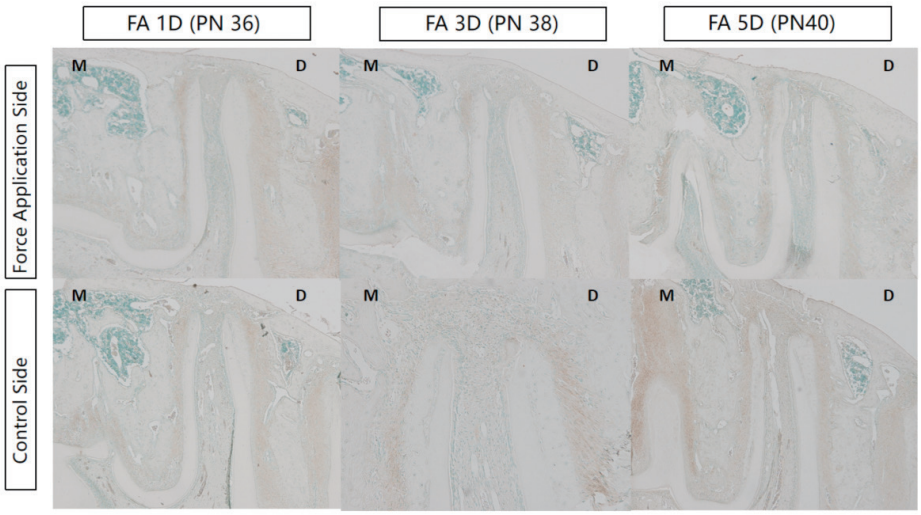

Fig.3 Immunohistochemistry of sclerostin after OTM. M, mesial side；D. distal side.

成果発表：（予定を含めて口頭発表、学術雑誌など）

1. The 9th International Orthodontic Congress, 2020 年 10 月 4 日 -11 月 3 日 , Online 開催
2. European Journal of Orthodontics 発表予定