研 究 者：CHEN YAOSEN
（所属：東京医科歯科大学 大学院医歯学総合研究科　咬合機能矯正学分野）

研究題目：Construction of animal MAC surgery model and mechanism of temporomandibular joint morphological change

Objective:

Mandibular autorotation concept (MAC) surgery is a novel approach for addressing long-term post-surgical stability in patients with skeletal mandibular retrusion and open bite resulting from temporomandibular joint osteoarthritis (TMJOA). However, research on MAC surgery animal models and the mechanisms underlying TMJ morphological changes is limited. This study aimed to establish an animal model for MAC surgery and elucidate the mechanisms driving TMJ morphological changes at histological and molecular levels.

Materials and methods:

A total of 36 female Wistar/ST rats (aged 5 weeks old) (Sankyo Lab Service, Tokyo, Japan), were divided into three groups: control group, bite-raise group, and recovery group (MAC surgery simulated group) (Fig. 1). In the recovery group, a 2.0 mm thick layer of composite resin (Light Cure, LC8001, Tomy Inc, Japan) was bonded to the upper molars at 5 weeks of age and removed at 13 weeks of age. In the bite-raise group, composite resin was bonded to the upper molars at 5 weeks of age and remained until the rats are sacrificed. The normal group served as the control. In each group, four rats were sacrificed at 13, 17, and 21 weeks of age, respectively. After composite resin bonded treatment, all groups' rats were simultaneously maintained on a soft diet (powder feed) with the same nutrient content as the normal diet. All animals were housed in the same room with controlled temperature, humidity, and light. A standard alternating 12 h light/dark cycle was maintained. The health status and body weight of the rats were monitored every other day. All animal experiments were performed with the approval of the Institutional Animal Care and Use Committee of TMDU (approval number: A2022-171A). All animals were used in compliance with the in vivo experiment (ARRIVE) 2.0 guidelines.

Micro-CT was employed to assess three-dimensional morphology and cancellous bone structure. Whole left mandible with condyle were fixed in 4% paraformaldehyde (pH 7.4) (Fujifilm Wako Pure Chemical Corp., Osaka, Japan) for 48 h at 4 ℃. Tissue samples were scanned using InspeXio SMX-100CT computed tomography system (Shimadzu Corp., Kyoto, Japan) and analyzed using a 3D trabecular bone analysis software (TRI/3D-BON-FCS; RATOC System Engineering Co., Ltd., Tokyo, Japan) according to the manufacturer's instructions. Trabecular bone was evaluated using the following parameters: bone volume

fraction (BV/TV, %), bone mineral density (BMD, mg/cm^3), bone surface ratio (BS/BV, per mm), trabecular thickness (Tb.Th, μm), trabecular number (Tb.N, per mm), trabecular separation (Tb.Sp, μm), and trabecular spacing (Tb.Spac, μm).

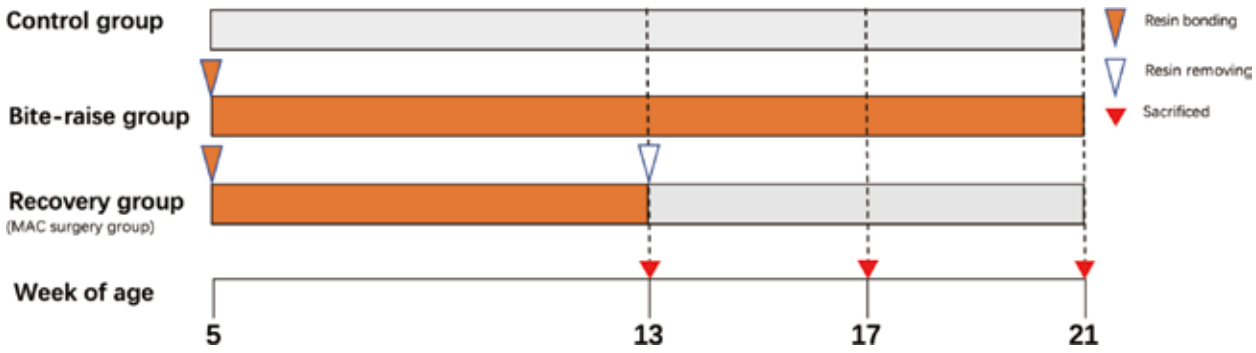

Fig. 1 Outline of experimental design

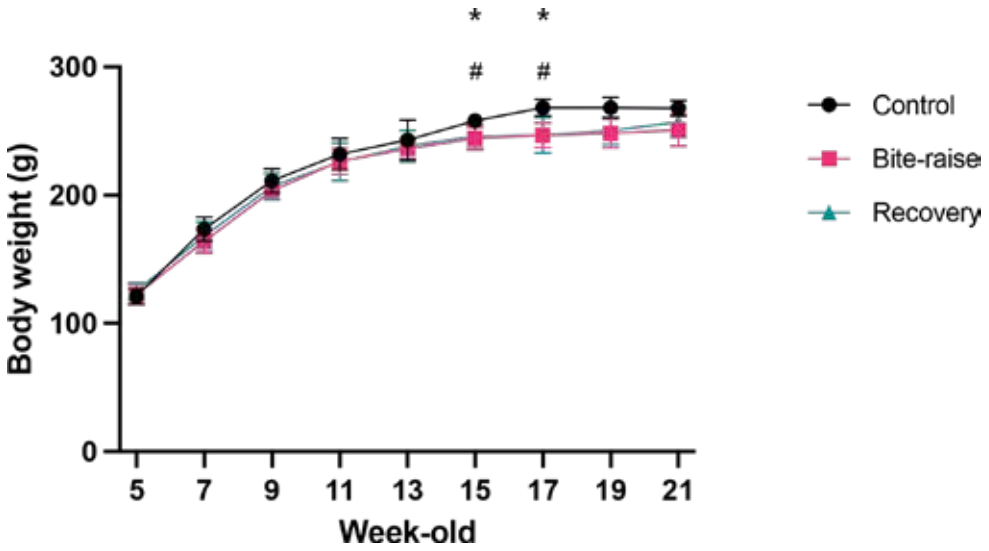

Fig. 2 Body weight changes from 5 week of age to 21 week of age. Values are presented as mean ± standard deviation. *: Control group vs. Bite-raise group, $p < 0.05$; #: Normal group vs. Recovery group, $p< 0.05$. 5-13 week-old: n=12; 15--17 week-old: n=8; 19--21 week-old: n=4.

Results:

No rat in the experimental period died of unexplained death, and they were well tolerated by the bite-raising. There was not significant difference been noted among 3 groups in terms of body weight changes except 15- and 17-week-old (Fig. 2).

Micro-CT images revealed significantly higher cortical and trabecular BMD in the Bite-raise and Recovery groups ($p < 0.05$) at 13 weeks of age (Fig. 3). Micro-structural bone analysis indicated that BV/TV was significantly lower in both the Bite-raise and Recovery groups compared to the Control group at 13 weeks of age ($p < 0.05$). (Fig. 4)The Bite-raise and Recovery groups also exhibited significantly higher Tb.Sp than the Normal group at 13 weeks of age ($p < 0.01$, $p < 0.05$, respectively).

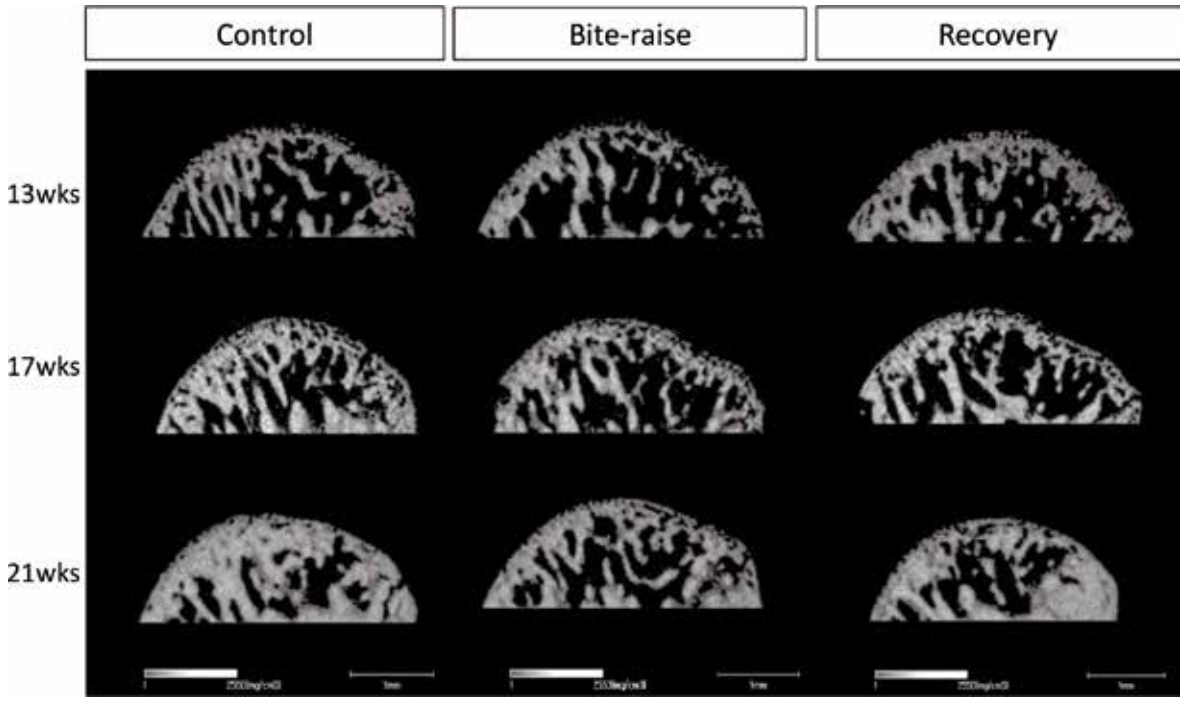

Fig. 3 Micro-CT images of the mandibular condylar head from the control, bite-raise and recovery groups in 13-, 17-, and 21 week-old. Abbreviation: 13wks, 13 weeks age; 17wks, 17 weeks age; 21wks, 21 weeks age.

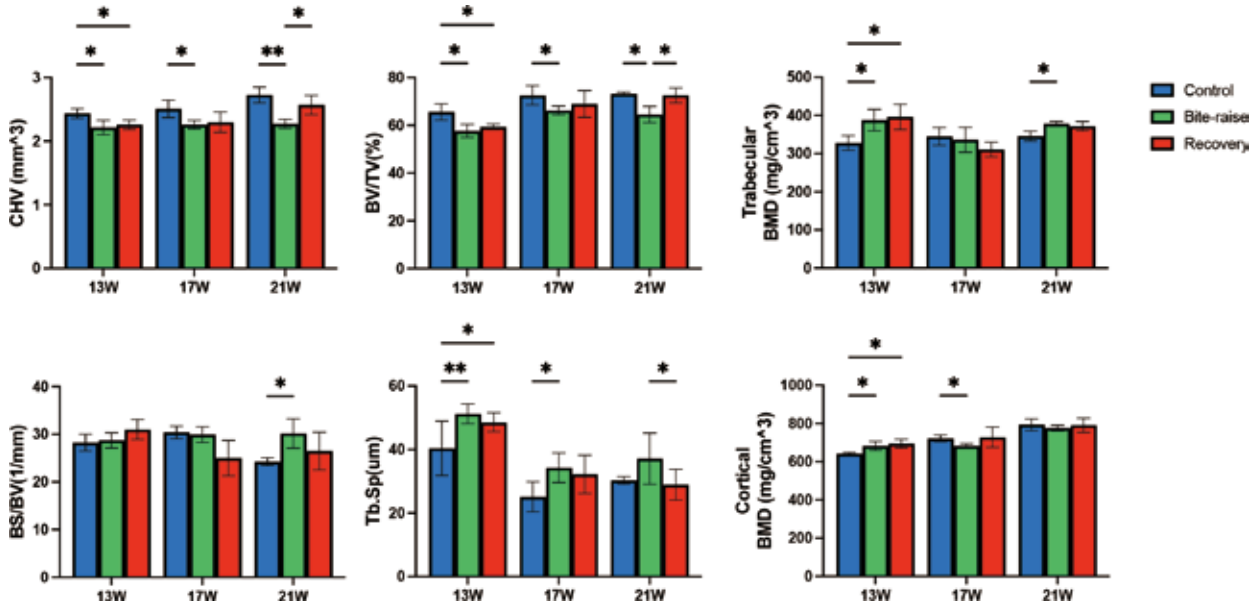

Fig. 4 Comparison of micro-CT analysis of BMD and architectural parameters. Abbreviations: CHV, condyle head volume; BV/TV, bone volume to tissue volume ratio; BMD, bone mineral density; BS/BV, bone surface to bone volume volume; Tb.sp, trabecular separation. Values are presented as mean ± standard deviation (n=4). $^{*}p < 0.05$, $^{**}p < 0.01$.

At 17 and 21 weeks of age, the Bite-raise group continued to display a significantly lower BV/TV value compared to the Control group, while the Recovery group did not show this difference. Conversely, a significantly higher BV/TV value was observed in the Recovery group at the 21-week time point ($p < 0.05$). A significant decrease in Tb.Th compared to the Control group was also noted at 21 weeks of age ($p < 0.05$).

Regarding Tb.Sp, the Bite-raise group was significantly higher relative to the Control and Recovery groups at 17 and 21 weeks of age, respectively, while no significant difference was noted between the Control and Recovery groups ($p > 0.05$). Additionally, the Bite-raise group exhibited significantly lower Tb.N and higher Tb.Spac values compared to the Control group at 17 weeks of age ($p < 0.05$) (Fig. 4).

Results publish:

- The results of this research are expected to be published at American Journal of Orthodontics and Dentofacial Orthopedics (AJO-DO) and Association American of Orthodontics annual conferences 2025 (AAO 2025).