論　文　内　容　要　旨

The dynamics of oral microbiome by fixed orthodontic appliances

(固定式矯正装置によって起きる口腔細菌叢変化)

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Background

The mouth is comprised of complex structure of hard and soft tissue such as teeth, tongue, gingiva, buccal mucosa and palate, then they have unique variations of microbiome structures according to the different surface properties. Full fixed orthodontic appliances are very common and effective tool to treat malocclusions but accompany with secondary effects. One of the important secondary effects is change of oral microbiome and subsequent infections caused by the appliances. Therefore, it has been pointed out the risk of white-spot lesions, dental caries or periodontal complication including gingivitis and periodontitis due to the change of oral microbiome. Almost all previous reports about the relationship between oral bacteria and orthodontic treatment focused on only specific species and very few reports focused on microbiome and its dynamics including commensal and unculturable bacteria followed by orthodontic treatment. The aim of this study is to assess the dynamics of oral microbiome caused by full fixed orthodontic appliances by 16S rRNA meta sequencing of supragingival plaque and saliva.

Materials and Methods

71 patients were selected for this study. All subjects participating in this study undergone orthodontic treatment by full fixed appliance during July 2016 - April 2018 at Department of Orthodontics, Hiroshima university hospital, Hiroshima, Japan. Supragingival plaque samples were collected at two time points: before placement (T0) and six months later after placement (T1). Saliva samples collected at three time points: (T0), (T1) and removal of appliances (T2). Microbial DNA was extracted from the plaque and saliva and library was prepared by tagmentation, purification, quantification and normalization for 16S rRNA meta sequencing. The sample library was applied to Miseq platform system (Illumina, CA, USA). The sequence data were analyzed by using Microbial genomics modules of CLC Genomics Workbench ver10(QIAGEN). Additional statistical analysis such as Wilcoxon signed-rank test and Kruskal-Wallis test were conducted by StatView 5.0J (SAS Institute, NC, USA).

Results

From the results of OTUs analysis and alpha diversity, the number of OTUs raised according to time shift both in plaque and saliva samples although there was no significant difference. Beta diversity exhibited the discrepancies of microbiome different time points especially in plaque samples. The taxonomic analysis at phylum level showed significant increase of *TM7* and decrease of *Proteobacteria* with time both in plaque and saliva. In plaque samples, the most dominant phylum both at T0 and T1 was *Proteobacteria* but

Bacteroidetes almost overtook other phyla. Main microbial distribution (more than 5.0% of relative abundance) in plaque at genus level were *Leptotrichia, Streptococcus, Capnocytophaga, Fusobacterium, Prevotella* and *Actinomyces*. Main microbial distribution in saliva samples at genus level were *Streptococcus, Neisseria, Haemophilus, Prevotella* and *Veillonella. Capnocytophaga, Fusobacterium* and *Leptotrichia* were more relatively abundant in supragingival plaque when compared with saliva. Conversely, *Neisseria* and *Haemophilus* were more abundant in saliva compare with supragingival plaque.

Genus *Prevotella, Capnocytophaga, Atopobium*, *Selenomonas* (including *S. noxia*) and *Campylobacter* significantly increased with time in both plaque and saliva. The species *Parvimonas micra and Solobacterium moorei* and the genus Gemella and Moyella showed significant increase with time not in saliva but in plaque. The genus *Fusobacterium, Tennerella, Leptotrichia* and *Paludibacter* significantly increased with time not in plaque but in saliva. These bacteria are all obligate anaerobe. Therefore, it is consistent in terms of the increase of periodontal pathogens and anaerobes both in plaque and saliva even though there are some differences of kind of bacteria.

The genus *Actinobacillus, Actinomyces, Corynrbacterium, Kingella* and *Neisseria* and the species *Haemophilus parainfluenzae, Lautropia mirabillis* and *Rothia dentocariosa* significantly decreased with time not in saliva but in plaque. The genus *Streptococcus* including *S. mutans* which is major pathogen of dental caries decreased with time both in plaque and saliva, although there was no significant difference. These changes suggested that periodontal pathogenic and anaerobic bacteria take the place of cariogenic and commensal bacteria in oral microbiome by full fixed orthodontic appliances.

Conclusions.

The oral microbiome of plaque and saliva changed during orthodontic treatment by full fixed appliances. The core dynamics of the oral microbiome was the increase of periodontal pathogens and the decrease of commensal bacteria.