Comparative analysis of alveolar bone resorption between male and female patient

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Abstract - **Alveolar bone resorption (ABR) occurs when bone deconstruction takes place in the areas surrounding and supporting a tooth. Traditional diagnostic methods to determine ABR include assessment of clinical parameters and radiographs; however, the current diagnostic techniques lack the capability to predict and assess future ABR occurrence among individuals. Both male and female walk-in patients visiting a local Japanese hospital throughout March 2017 were selected for this study. For fair comparison, all samples were collected focused on the primary molar. Radiographs of the alveolar bone and tooth were taken for diagnostic purposes. From this study, it was established that the alveolar bone matrix is affected by both sex and age. More specifically, box plot analyses show that: alveolar bone matrix is affected by both sex and age; female and male alveolar bone development peaks at the 40s and 50s age group, respectively; female alveolar bone resorption start[s] at the 50s age group, and male alveolar bone resorption starts at the 60s age group.**

Key Words: alveolar bone resorption (ABR); BoneJ; radiographs

INTRODUCTION

I. Background

Alveolar bone/ process is an elevated ridge of the maxima, or mandible where the teeth are housed. [1] There are two components which are alveolar process and alveolar bone proper. Alveolar process is formed to house the developing tooth buds and roots of the teeth. Alveolar bone proper is the portion of bone that lines the tooth socket. There are three different sections in an alveolar bone, which are upper interradicular septum (UIS), middle interradicular septum (MIS) and lower interradicular septum (LIS). Each section has a different densities of alveolar bone matrix.

Alveolar bone resorption (ABR) is the destruction of bone in the areas surrounding and supporting a tooth.[2]Besides, ABR has been associated with oral hygiene and age of the individual, wherein, individuals with poor oral hygiene developing periodontal disease exhibit more ABR while aging individuals slowly and gradually develop ABR. [3]

II. Significance

Alveolar bone health is often neglected, however, the state of the alveolar bone as someone ages may have an impact in one's future health since it could indirectly affect the type and amount of food one will ingest. In this regard, establishing the age-related pattern of alveolar bone matrix could similarly guide dental practitioners in knowing the specific age-related health of the alveolar bone matrix during dental procedures. Moreover, by having establish the age-related AB matrix, dental practitioners may likewise be guided in diagnosing early onset ABR and, subsequently, appropriate therapeutic treatment can be performed immediately.

III. Objective

Currently, traditional diagnostic methods to determine ABR include assessment of clinical parameters and radiographs; [4]however, these conventional techniques are limited since only a historical perspective (not the present and actual appraisal) is used to establish ABR and, more importantly, current diagnostic techniques lack the capability to predict and assess future ABR occurrence among individuals.[5] Gingival crevicular fluid (GCF) is a physiological fluid that is excreted from the gingiva and usually builds up between the dental-gingival space. In the advent of the 21st century, advances in the use of oral fluids (such as the GCF) as possible sources of disease biomarkers are becoming popular since oral fluids contain several mediators often associated with several diseases and disease manifestations, including ABR. However, at present, prospects of using GCF as an indicator of ABR have never been elucidated. In this regard, I hypothesize that certain components found in the GCF have the potential to be used as a biomarker to determine and predict ABR occurrence among individuals.[6] [7]

METHODOLOGY

IV. Patient Selection

Ethical approval was obtained from the local ethics committee prior to the start of this study. Both male and female walk-in patients (n=39) visiting a local Japanese hospital throughout March 2017 were used (Figure 1). A nonprobability purposive sampling was performed to satisfy the study requirements concerning sex and age. Male and female patients were grouped and at least 3 patients per age group (the 20s, 30s, 40s, 50s, 60s, 70s) were utilized. Age groups were divided by 10 to reflect the patients age that visited during the collection timeframe. Number of patients used for the study is dependent on patient check-in during the designated collection time-frame. All patients were informed that their participation was voluntary, and consent was obtained from each participating patient. Among the selected patients based on age and sex, patients were further subdivided into patients with healthy tissue and patient with periodontal disease. Patients who are smokers, or on an antibiotic regimen, or anti-inflammatory drugs (except for the elderly volunteers) were disqualified from this study.

V. Sample selection

For comparison, all samples collected focused on the primary molar, and probing depth was measured for periodontal tissue examination. Radiographs of the alveolar bone and tooth were taken for diagnostic purposes and results were used for the study. Similarly, GCF was collected using a paper point inserted at 6 different locations of the tooth. Both radiography and GCF collection were performed in all patients following the same timeframe (between 9:00-11:00 AM) prior to any treatment.

Patient type	Patient number (n)
Healthy Tissue	Female: n=21; Male: n=18
Periodontal Disease	Female: n=4; Male: n=2

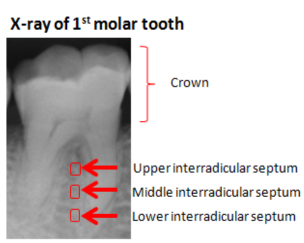

Figure 1. Patient selection and sample collection. Upper (UIS), Middle (MIS), and Lower (LIS) interradicular septum are indicated.

VI. Alveolar bone assessment

AB matrix across the age groups, between sexes, and oral condition comparison were determined using the radiograph from each patient and analyzed using BoneJ software (a specialized software used to measure bone matrix).

VII. Biochemical analyses.

Representative cellular stress [oxidative stress: total heme, H_2O_2; nitrosative stress: nitric oxide; ER stress: GADD153][9][10] and cell signaling [substance P[11], calcium[12], NF-κB[13]] [14] components were measured using commercially available kits. [15]

IX. Comparative analysis

Radiographs and GCF samples from subdivided patients with the same sex[16] and age[17][18] were compared to one another in order to establish the possible differences and potential disease markers with therapeutic applications.

RESULTS AND DISCUSSION

Throughout this study, both computational and biochemical approaches were performed in order to establish the age-related differences in the AB matrix. Computational approach (BoneJ) was utilized to establish the differences among UIS, MIS, and LIS between the different age groups. Biochemical approaches (stress and cell signaling) were performed to determine any biochemical patterns that may be associated with variations in AB matrix.

X. Interradicular septum varies between age groups and sex

As seen in Figure 2, the surface plot color and measurement among the interradicular septums (UIS, MIS, LIS) and age (20s-70s) varies. [17] In regards to the interradicular septum (vertical data), the interradicular septum is found between the molar roots and is further subdivided into 3 parts with the UIS being closest to the crown, MIS position underneath the UIS, and LIS located farthest from the crown, but closer to the jaw bone. Among the varying age groups, it is evident that UIS has the lowest AB density, MIS has an intermediate AB density, and LIS has the highest AB density. Overall, this is consistent with how the tooth molar functions. In a chewing scenario, the function of the tooth molar is to grind and breakdown food which in-turn would mean high amounts of physical stress (related to bite force) within the AB matrix. Having a softer UIS would allow for the AB matrix to absorb most of the physical stress related to chewing. Subsequently, the MIS serving as an intermediary between the UIS and LIS may partially function in absorbing physical stress and at the same time hold the tooth molar in place. Ultimately, the LIS may serve as the base thereby provide a solid foundation to hold the tooth molar in place.

In regards to the observed age-related AB matrix variation (horizontal data), it is apparent that the older the patient the AB matrix in the UIS, MIS, and LIS changes. This would suggest that the AB changes as the aging process progresses in both female and male patients. It is possible that at 20s, AB is not fully developed which may explain why there is lower AB density (yellow to yellow green color). Surprisingly, comparing the AB between female and male individuals;the estimated AB matrix (dark green to blue color) is highest during the 30s and 40s among aging female patients, whereas, among aging male patients, estimated AB matrix is highest during the 40s and 50s. This would imply that the AB matrix density is fully developed at these age groups. Interestingly, after obtaining the highest AB matrix measurement, there seems to be a tendency to dip (50s-60s) and eventually rise again (60s-70s), particularly among the elderly aged group (60s and 70s) which could be due to tooth loss among the elderly population, whereby, loss of tooth among the elderly would in-turn solidify the AB matrix thereby increasing its density Taken together, these results would suggest that: (1) the AB matrix differs between sex and aged groups; and (2) the AB matrix development peaks at the 30s-40s age group for females and 40s-50s age group for males.

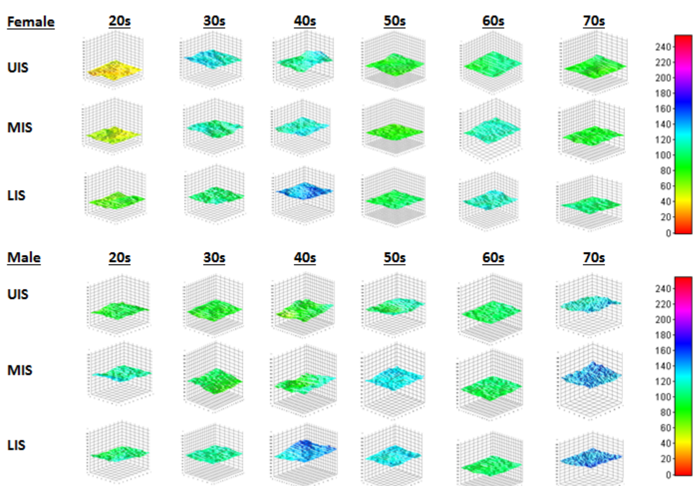

Figure 2. Alveolar bone matrix of female and male patients differs. Color legend representing the alveolar bone matrix is indicated on the right. Color gradient going up the legend represents higher alveolar bone density. Color gradient going down represents lower alveolar bone density.

XI. Stress and cell signaling related to bone resorption varies among age and sex

There are various types of cellular stresses occurring in a cell[18], among them: oxidative stress, nitrosative stress, and endoplasmic reticulum stress. Oxidative stress represents an imbalance between pro-oxidant and anti-oxidant activities, nitrosative stress is caused by the reaction of nitric oxide with oxygen or superoxide resulting in the formation of reactive nitrogen species with varying reactivity that could directly affect cellular enzyme activity, and ER stress is considered a cellular response activated when unfolded proteins accumulate within the ER in order to preserve ER function. Cellular stress have been correlated to age-related diseases and considering ABR is age-related it is possible that cellular stress (via oxidative, nitrosative, and/or ER stresses) along the GCF may contribute to ABR induction.

For this study, we established oxidative stress occurrence by measuring both total heme and H_2O_2. Similarly, we established nitrosative stress by measuring the amount of nitric oxide. Finally, we established ER stress by measuring the amount of GADD153. All these biochemical components used for this study are known biomarkers for all 3 cellular stresses, respectively.

Subsequently, cellular stress is known to trigger other physiological cell signals that have been associated with bone resorption, such as: substance P, calcium, and NF-κB. Substance P has been associated with osteoclastic bone cells responsible for breaking down bone tissues, whereas, calcium signaling is known to directly trigger bone resorption. Moreover, NF-κB is known to activate osteoclast-related bone resorption. Thus, all these cell signals are known biomarkers of bone resorption.

In general, among the biochemical components studied (Figure 3), a common bi-modal distribution (40s:60s age group) can be observed in all male patients studied across age groups (*indicated in blue*). In contrast, among female patients studied across age groups (*indicated in red*), multiple sets of bi-modal distribution is observed: 30s:50s; 40s:70s; and 50s:70s age groups. These results would suggest that GCF components and production are consistent in male patients throughout the ageing process, whereas, among female patients, GCF components and production have a tendency to shift as the ageing process progresses.

Admittedly, all data sets are based on theoretical and computational analysis of actual patient diagnosis. Moreover, the collection timeframe is short and collection site was limited to one. As a possible future study, expanding both collection timeframe and site may provide a better overview of the age-related differences in alveolar bone matrix. Additionally, considering all volunteer patients were Japanese, expanding the study to include other nationalities could be another aspect to explore.

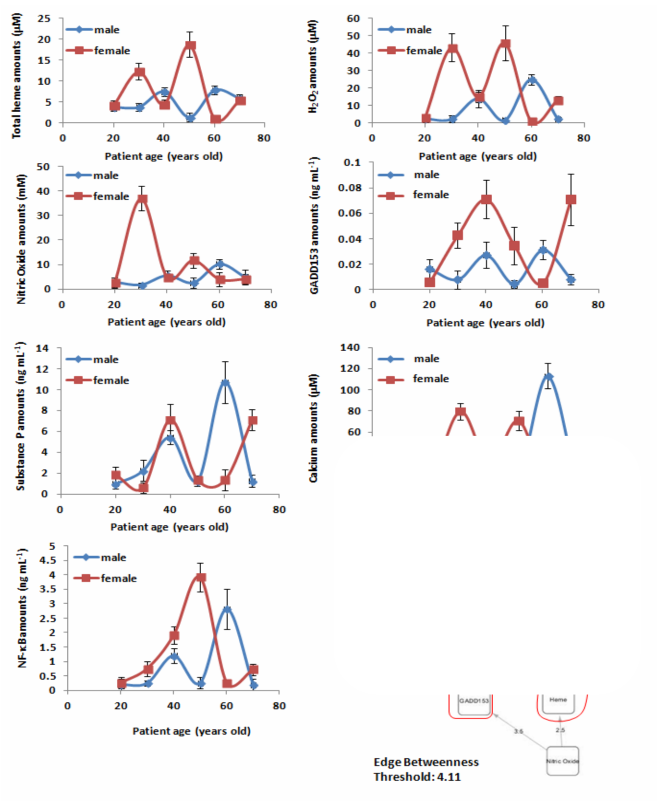

Figure 3. GCF cellular stress and stress-related signaling components in female and male patients differ. Stress signaling networks are boxed red.

CONCLUSION AND IMPLICATIONS

In summary, these results suggest that: (1) alveolar bone matrix is affected by both sex and age; (2) female and male alveolar bone development peaks at the 40s and 50s age group, respectively; (3) female alveolar bone resorption start at the 50s age group, and (4) male alveolar bone resorption starts at the 60s age group.

As a possible clinical application, these results demonstrate that certain GCF components could serve as biomarkers for the early diagnosis and treatment of ABR. Moreover, the proposed AB matrix pattern may likewise serve as a reference or guide for dental practitioners when performing procedures or treatment involving AB, such as root canals, implants, and braces.

ACKNOWLEDGMENTS

I would like to express my gratitude to my primary supervisor, Dr. Marni Cueno, who guided me throughout this project. I would also like to thank the Nihon University School of Dentistry for providing radiographs used throughout this study.

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