

# Time-dependent Changes in Occlusal Status in an Implant-supported Prosthesis at the Mandibular First Molar from Prosthesis Placement to 3 Months After

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## ABSTRACT

**Aim:** The purpose of this study was to elucidate time-dependent changes in occlusal status over a 3-month period to understand dynamic factors that act on implant-supported prosthesis. We used pressure-sensitive film for occlusal force diagnostics and silicone testing material to measure the occlusal status of a mandibular first molar implant-supported prosthesis under controlled clenching strengths.

**Materials and methods:** The subjects were eight patients who had an implant-supported prosthesis inserted at the mandibular first molar and did not have any missing teeth other than the implants. We performed the following tests immediately and 3 months after fitting the prosthesis. First, we monitored masseter muscle activity and defined maximum clenching strength as 100% maximum voluntary contraction (MVC). We then used pressure-sensitive film and a clenching strength measuring device to measure occlusal load and occlusal contact area at clenching strengths of 40, 60, 80, and 100% MVC. Finally, we used silicone testing material and an occlusal contact measurement device to measure occlusal contact area at clenching strengths of 20, 40, and 60% MVC.

**Results:** Occlusal load and occlusal contact area of the bilateral molar region increased at all clenching strengths 3 months after fitting the prosthesis. However, the quotient of bilateral molar occlusal contact area divided by occlusal load (contact area/load) showed no significant changes after 3 months for any of the clenching strengths. There was also no significant change observed in occlusal load of the prosthesis, occlusal contact area of the prosthesis and contact area/load significantly

**Conclusion:** Wearing an implant-supported prosthesis for 3 months increased clenching strength, which increased the overall bilateral molar occlusal contact area and occlusal load. Our findings suggest that implant-supported prostheses increase occlusal contact area at high clenching strengths after 3 months of use.

**Clinical significance:** This study suggested that implant-supported prosthesis which have ideal occlusal contact status need to be checked and occlusal status adjusted regularly for its prediction.

**Keywords:** BiteEye, Clenching strength, Cohort study, Implant, Occlusal contact area, Occlusal load, Occluzer, Time-dependent change.

**How to cite this article:** Terazawa M, Sato Y, Kitagawa N, Osawa T, Imamura Y. Time-dependent Changes in Occlusal Status in an Implant-supported Prosthesis at the Mandibular First Molar from Prosthesis Placement to 3 Months After. *Int J Prosthodont Restor Dent* 2018;8(2):44-53.

**Source of support:** Nil

**Conflict of interest:** None

## INTRODUCTION

Implant therapy has developed into a highly predictable treatment method with the establishment of placement protocols and improvements in fixture surface texture and fixture forms. However, various procedural accidents, such as an implant-supported prosthesis fracture, screw loosening, alveolar bone resorption, and disintegration have also been reported. One factor believed to have a high impact on procedural issues is overload after fitting the an implant-supported prosthesis.<sup>1,2</sup> It is therefore, important to determine the optimal occlusal status by wearing a provisional restoration before setting the final prosthesis in implant therapy. Overload on an implant-supported prosthesis has also been reported to induce peri-implant inflammation years after beginning occlusal loading.<sup>3</sup>

In cases where natural teeth and implants are both present, natural teeth and implants undergo different phases of changes in the jaw when subjected to occlusal force. It is conceivable that differences in displaceability characteristics between natural teeth and implants cause variation between their respective occlusal statuses when clenching at lower and higher strengths, thereby causing dynamic disequilibrium.<sup>4,5</sup> Therefore, some theorize that occlusion on an implant-supported prosthesis should be made lower compared with natural teeth according to the thickness of the periodontal membrane to complement displacement differences.<sup>6-8</sup> Conversely, others believe that equal occlusion should be applied to the implant-supported prosthesis and surrounding natural teeth.<sup>9</sup> Thus, results are inconclusive regarding the optimal occlusal status that should be applied to implant-supported prostheses.

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Previously in this field, Okuyama et al<sup>10</sup> used pressure-sensitive film for occlusal force diagnostics to elucidate the occlusal status of natural teeth and implants and demonstrated good ability to calculate the mean value of the ideal occlusal clearance. Imamura et al<sup>11</sup> developed a method to examine changes in the occlusal status between low and high clenching strengths in individuals with natural dentition by using a new silicone testing material and pressure-sensitive film for occlusal force diagnostics. Imamura et al<sup>11</sup> confirmed that these methods were also effective for implant-supported prostheses. At the same time, they suggested that occlusal contact area and occlusal load of an implant-supported prosthesis at the mandibular first molar were decreased compared with that of the same number of teeth on the contralateral side even when clenching strength increased.

In light of these findings, the purpose of the present study was to elucidate time-dependent changes in the occlusal status of an implant-supported prosthesis at the mandibular first molar with using pressure-sensitive film for occlusal force diagnostics, an occlusion measurement device, silicone testing material, and an occlusal contact measuring device under clenching strength controlled conditions visual feedback method.

## MATERIALS AND METHODS

### Subjects and Their Dentition

The subjects were 8 patients (3 men, 5 women) aged 34 to 66 years ( $50 \pm 10.8$  years) treated at Showa University Dental Hospital (Table 1). The subjects' implants were placed on the central missing portion of the mandibular first molar and fitted with a fixed implant-supported prosthesis (hereinafter, the prosthesis) (screw-ins, single implant). Selection criteria were as follows<sup>12,13</sup>:

- Absence of inflammation (redness, swelling) at the implant placement site
- Absence of implant instability
- Absence of subjective symptoms, such as pain or discomfort
- Absence of significant bone resorption visible in X-ray images

**Table 1:** Subject profiles

Sex	Age (years)	Implant system	Implant site
F	53	Brånemark	Left
F	54	Straumann	Right
F	38	Straumann	Right
M	48	Brånemark	Left
M	65	Brånemark	Right
F	48	Straumann	Left
F	34	Straumann	Left
M	66	Straumann	Left

The criteria for subjects' dentition were as follows:

- All teeth other than the subject tooth (the implant) present as natural teeth, with 28 teeth from the medial incisors to the second molar, including the implant
- Absence of tooth instability and no pocket depths  $\geq 4$  mm upon basic periodontal examination
- Absence of history of orthodontic treatment
- Absence of temporomandibular joint arthrosis or masseter muscle pain, mandibular movement anomalies, and other symptoms of oromandibular functional abnormalities
- Presence of at least one occlusal contact point of the prosthesis at maximum clenching

During the survey period, 34 patients who fulfilled the above conditions were recruited, 22 of whom consented to the study. Of these patients, data were obtained from 13 subjects immediately after fitting the prosthesis while data after 3 months were only obtained in eight subjects. Six subjects had at least one site of occlusal contact on the prosthesis at maximum clenching, and we compared and evaluated time-dependent changes based on the data of these six subjects. Measurements were taken on the day of setting the prosthesis after adjusting the occlusion (baseline) and 3 months after fitting the prosthesis.

This study was approved by the institutional review board of the ethical committee of Showa University, Department of Dentistry (approval no. 2012-020). All subjects gave their consent before the study was started after receiving a sufficient description of the purpose and methods of this research.

### Setting Maximum Clenching

Electromyography (Power Lab, AD instrument, Nagoya, Japan) was used to measure masseter muscle activity. Silver disk electrodes measuring 10 mm in diameter (Duotrode; Morita Corp., Osaka, Japan) were adhered to both sides of the central part of the masseter muscle with bipolar leads. The distance between electrodes measured 21 mm, and the electrodes were placed parallel to the direction in which the masseter muscle fibers run.

We defined 100% MVC as masseter muscle activity at maximum clenching strength of subjects without anything interposing between the upper and lower teeth. Subjects were shown visual feedback that allowed them to see the muscular force exerted in numerical values.

### Measurement and Analysis of Subjects' Dentition

#### Measurement of Occlusal Load and Occlusal Contact Area using Pressure-Sensitive Film

Pressure-sensitive film (Dental Prescale 50H type R<sup>®</sup>; Fuji Photo Film Co., Tokyo, Japan) for occlusal force diagnostics was used to examine occlusal contact area and occlusal

load in the intercuspal position simultaneously. Masseter muscle activity (clenching strength) was measured at 40, 60, 80, and 100% MVC, and subjects were measured three times at each of these clenching strength intensities using visual feedback. Subjects were seated with their heads resting on the headrest of the dental unit to set the occlusal plane parallel to the floor. Subjects were instructed to open their mouths at one finger's width, close their mouths after slowly inserting Prescale, and then clench their teeth together. Prescale was interposed between the full dentition between the second molars on either side, and subjects were instructed to bite in the intercuspal position. They were asked to clench on Prescale for 3 seconds. To avoid muscular fatigue, 5-minute intervals were inserted between measurements.<sup>7</sup> Prescale was stored in a cool, dark place for 24 hours,<sup>12</sup> and the colored parts, their surface area, and their color density were analyzed using a specialized analysis apparatus (Occluzer FPD707<sup>®</sup>; Fuji Photo Film Co. Tokyo, Japan). Occlusal force was analyzed by a software program (DePROS-PC<sup>®</sup>; GC, Tokyo, Japan) and converted to pressure values to calculate occlusal load and occlusal contact area in the molar regions.

#### *Measurement of Occlusal Contact Area using Silicone Testing Material*

Silicone testing material (Blue Silicone<sup>®</sup>, GC, Tokyo, Japan) was used to test occlusal contact in the intercuspal position. The visual feedback method was used to set clenching strength at 20, 40, and 60% MVC, and Blue Silicone was used to measure occlusal contact area at each clenching strength intensity. Subjects were placed in the same position as for Prescale measurement and instructed to keep their mouths open at one finger's width. Blue Silicone was inserted on the lower teeth and held in the mouth for 15 seconds, after which subjects were asked to clench their teeth for 30 seconds while maintaining the prescribed clenching strength using the visual feedback method. They stayed in the same position for another 30 seconds until Blue Silicone completely solidified. Subjects were allowed to rest at 5-minute intervals between measurements to prevent muscular fatigue. Data obtained by Blue Silicone were analyzed using BiteEye (BiteEye-I<sup>®</sup>, GC Tokyo, Japan) for occlusal contact measurement.

#### **Analysis of Results obtained by Occluzer and BiteEye**

The following items were calculated and compared at baseline and after 3 months:

- Occlusal contact area and occlusal load of the prosthesis
- Occlusal contact area and occlusal load of the same number of teeth on the contralateral side (hereinafter, the contralateral tooth)

- Occlusal contact area and occlusal load in the region between the first premolar to the second molar in the lower jaw (hereinafter, bilateral molar region) including the prosthesis
- Ratio of occlusal contact area and occlusal load of the prosthesis over the total bilateral molar region
- Ratio of occlusal contact area and occlusal load of the contralateral tooth over the total bilateral molar region
- Occlusal contact area of the prosthesis divided by occlusal load
- Occlusal contact area of the contralateral tooth divided by occlusal load
- Occlusal contact area of the bilateral molar region divided by occlusal load.

#### **Statistical Analysis**

For items 1 to 5, two-way analysis of variance (ANOVA) was performed. The dependent variables included occlusal loads and contact areas of the prosthesis, contralateral tooth, and bilateral molar region and ratios of load and area of the prosthesis and the contralateral tooth over the bilateral molar region. Intrasubject factors were measurement time and clenching strength. The Wilcoxon signed-rank test was then used to test for differences at each clenching strength intensity in each region. For items 6 to 8, we performed a two-way ANOVA with values obtained by dividing occlusal contact area of each region by occlusal load as dependent variables and measurement time and clenching strength as intrasubject factors. Significant differences at each clenching strength intensity in each region were determined using the Wilcoxon signed-rank test. All statistical analyses were conducted using PASW Statistics 23 (SPSS, Tokyo, Japan); p-values <0.05 were considered statistically significant.

## **RESULTS**

### **Analysis of Blue Silicone and Prescale (for Subject 6)**

Representative results of analysis of Blue Silicone with BiteEye (Fig. 1) and Prescale with Occluzer (Graph 1) are shown for Subject 6.

### **Time-dependent Changes in the Prosthesis**

#### *Occlusal Contact Area*

The Wilcoxon signed-rank test indicated that occlusal contact area of the prosthesis increased with greater clenching strength at 3 months after fitting the prosthesis ( $p \leq 0.05$ ) (Graph 2). Occlusal contact area significantly increased after 3 months at 40% MVC clenching strength with BiteEye and 100% MVC clenching strength with Occluzer ( $p \leq 0.05$ ). Two-way ANOVA indicated that occlusal contact area of

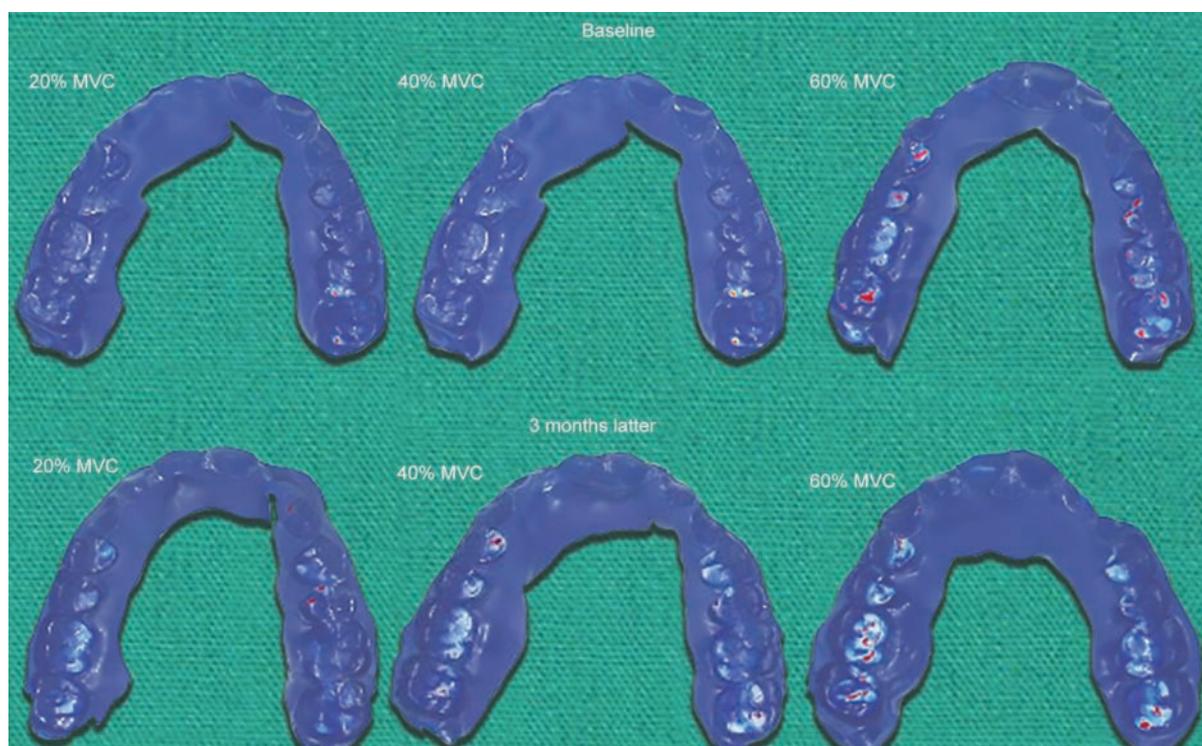
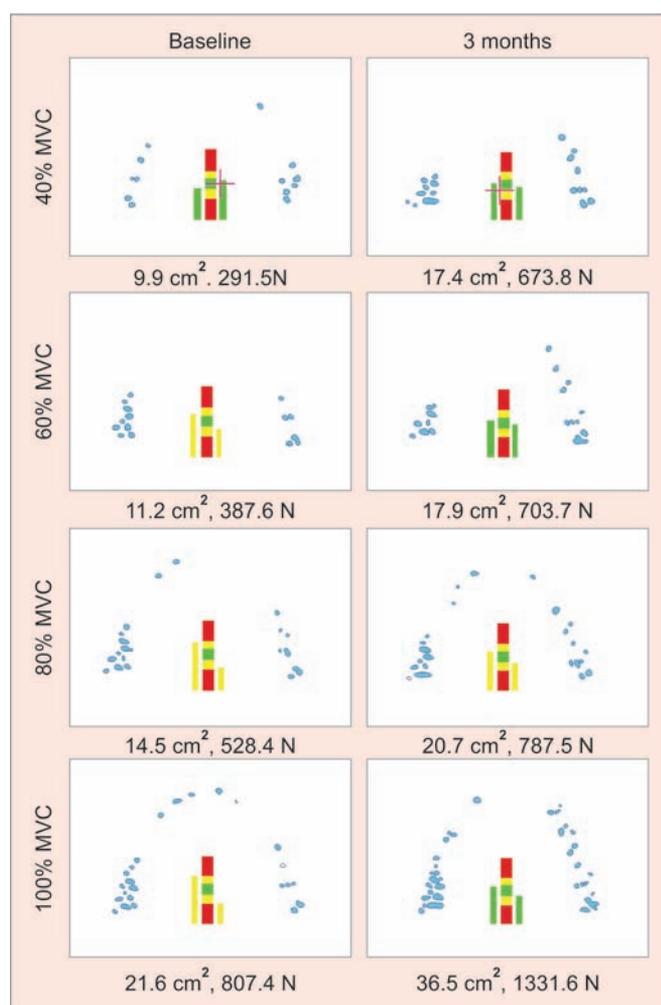


Fig. 1: Representative results of analysis of occlusal contact area with Blue Silicone in subject 6



Graph 1: Representative results of analysis of occlusal contact area/load with prescale in subject 6

the prosthesis was not significantly different after 3 months with both BiteEye and Occluzer ( $p > 0.05$ ).

#### Occlusal Load

Occlusal load of the prosthesis increased with increasing clenching strength both at baseline and 3 months after setting the prosthesis (Graph 2). However, no significant differences were observed for any of the clenching strength intensities ( $p > 0.05$ ). Two-way ANOVA also indicated no significant difference between baseline and 3-month values after setting the prosthesis ( $p > 0.05$ ).

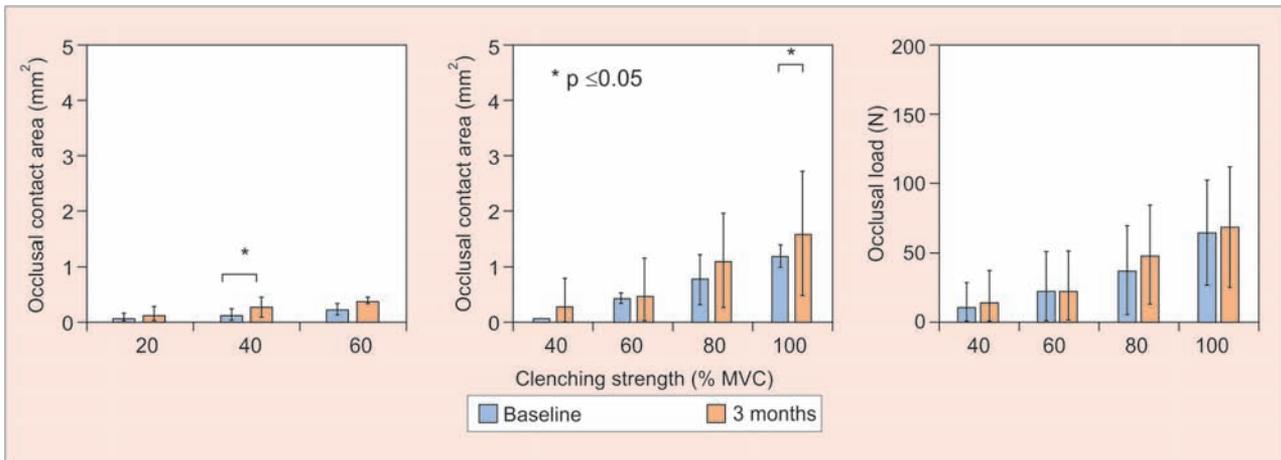
#### Time-dependent Changes in the Contralateral Tooth

##### Occlusal Contact Area

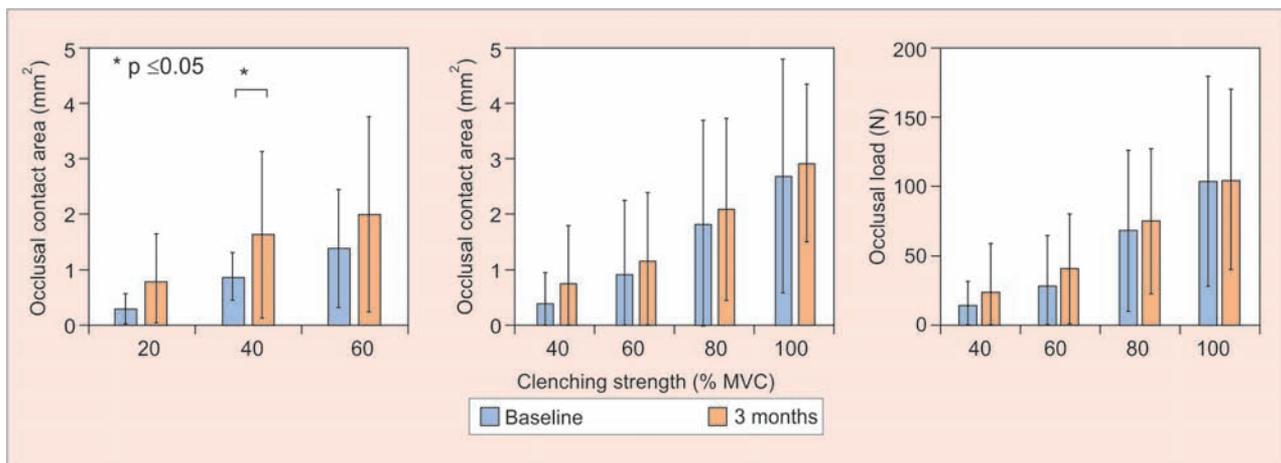
Occlusal contact area of the contralateral tooth increased with greater clenching strength both at baseline and 3 months after setting the prosthesis (Graph 3). Occlusal contact area of the contralateral tooth significantly increased after 3 months with BiteEye at 40% MVC clenching strength ( $p \leq 0.05$ ). Two-way ANOVA revealed that occlusal contact area of the contralateral tooth did not change significantly at baseline compared with 3 months with BiteEye or Occluzer ( $p > 0.05$ ).

##### Occlusal Load

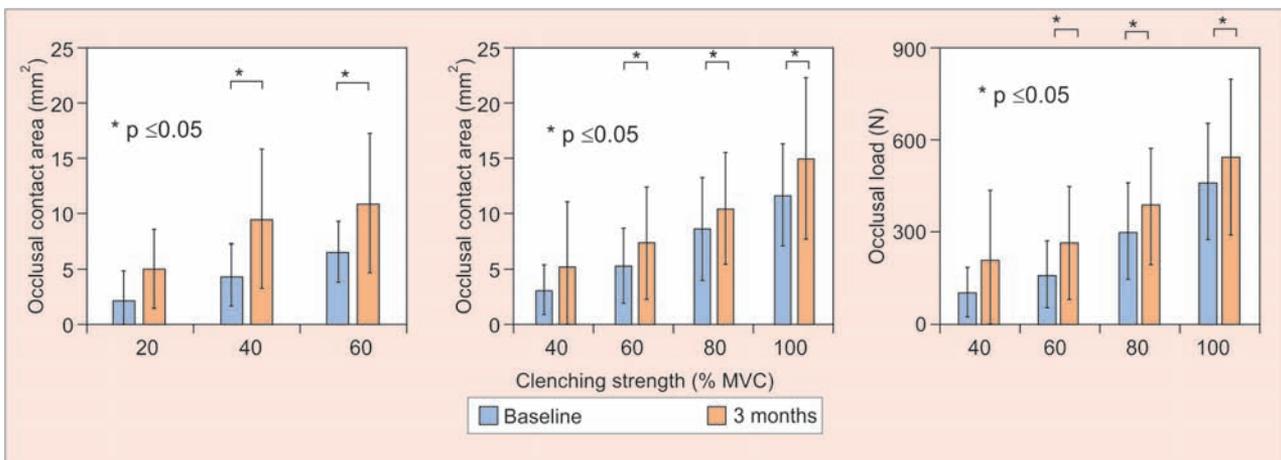
Occlusal load of the contralateral tooth increased with greater clenching strength both at baseline and 3 months



**Graph 2:** Time-dependent change of occlusal contact area and load of the prosthesis



**Graph 3:** Time-dependent change of occlusal contact area and load of the contralateral tooth



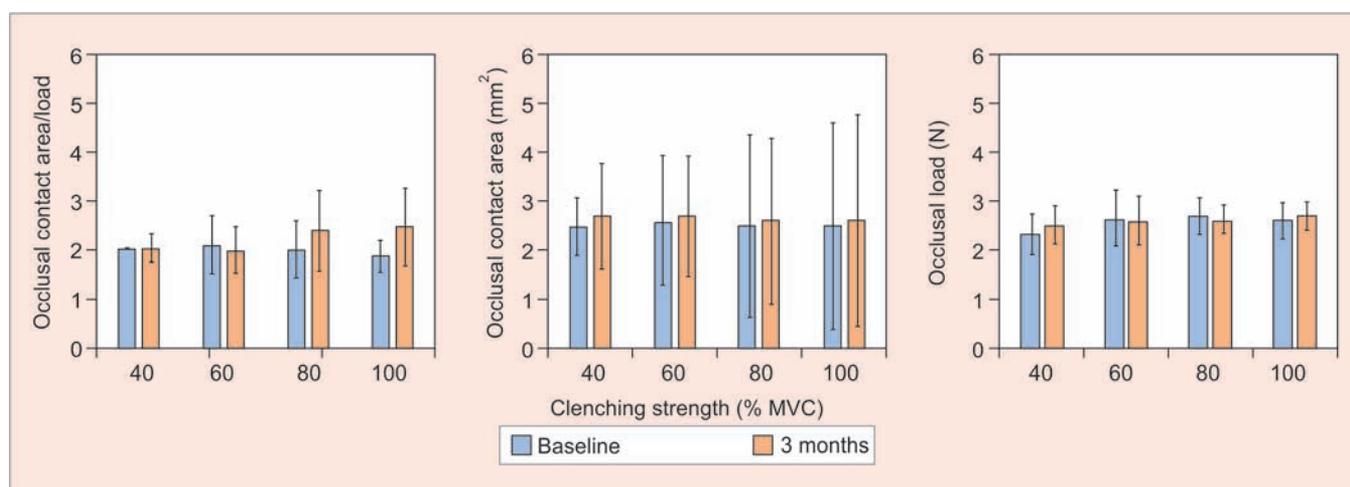
**Graph 4:** Time-dependent change of occlusal contact area and load of the bilateral molar region

after setting the prosthesis (Graph 3). There was no significant difference between baseline and 3-month values at any clenching strength intensity ( $p > 0.05$ ). Two-way ANOVA indicated that there was no significant difference in occlusal load of the contralateral tooth at baseline and 3 months ( $p > 0.05$ ).

### Time-dependent Change in the Bilateral Molar Region

#### Occlusal Contact Area

Occlusal contact areas of the bilateral molar region increased with greater clenching strength both at baseline



**Graph 5:** Time-dependent change of occlusal contact area/load of each region

and after 3 months (Graph 4). Significant increases in the bilateral molar region occlusal contact areas with BiteEye at 40 and 60% MVC clenching strengths and Occluzer at 60, 80, and 100% MVC clenching strengths were observed ( $p \leq 0.05$ ). However, two-way ANOVA indicated that there was no significant difference observed between baseline and 3-month values with both BiteEye and Occluzer ( $p > 0.05$ ).

#### Occlusal Load

Occlusal load in the bilateral molar region increased with greater clenching strength at baseline and 3 months (Graph 4). Occlusal load significantly increased after 3 months at clenching strength intensities of 60, 80, and 100% MVC ( $p \leq 0.05$ ) (Graph 2). However, two-way ANOVA indicated no significant difference between baseline and 3-month values for occlusal load of the bilateral molar region ( $p > 0.05$ ) (Graph 4). Furthermore, the maximum occlusal load of the bilateral molar areas increased by an average of  $15 \pm 10.3\%$  in all subjects from baseline to 3 months.

#### Quotient of Bilateral Molar Occlusal Contact Area Divided by Occlusal Load (Hereinafter, Occlusal Contact Area/Load) and Relationship Between Occlusal Contact Area and Occlusal Load (Hereinafter, Occlusal Contact Area–Load) of Each Region

##### The Prosthesis

Occlusal contact area/load was approximately 2.0% at baseline, irrespective of clenching strength (Graph 5). Furthermore, after 3 months, occlusal contact area/load remained constant at 2.0% at clenching strength intensities of 40 and 60% MVC, but increased to 2.4% at clenching strength intensities of 80 and 100% MVC. Occlusal contact

area/load significantly increased after 3 months at 100% MVC clenching strength ( $p \leq 0.05$ ) (Graph 5). Two-way ANOVA indicated no significant difference between baseline and 3-month values ( $p > 0.05$ ). Occlusal contact area–load is shown in Graph 6. Occlusal contact area–load increased between clenching strengths of 80 and 100% MVC.

##### The Contralateral Tooth

Occlusal contact area/load of the contralateral tooth was 2.5% at both baseline and 3 months for all clenching strength intensities (Graph 3). There was no significant difference between baseline and 3-month values at all clenching strength intensities ( $p > 0.05$ ). Two-way ANOVA also revealed no significant difference between baseline and 3-month values ( $p > 0.05$ ).

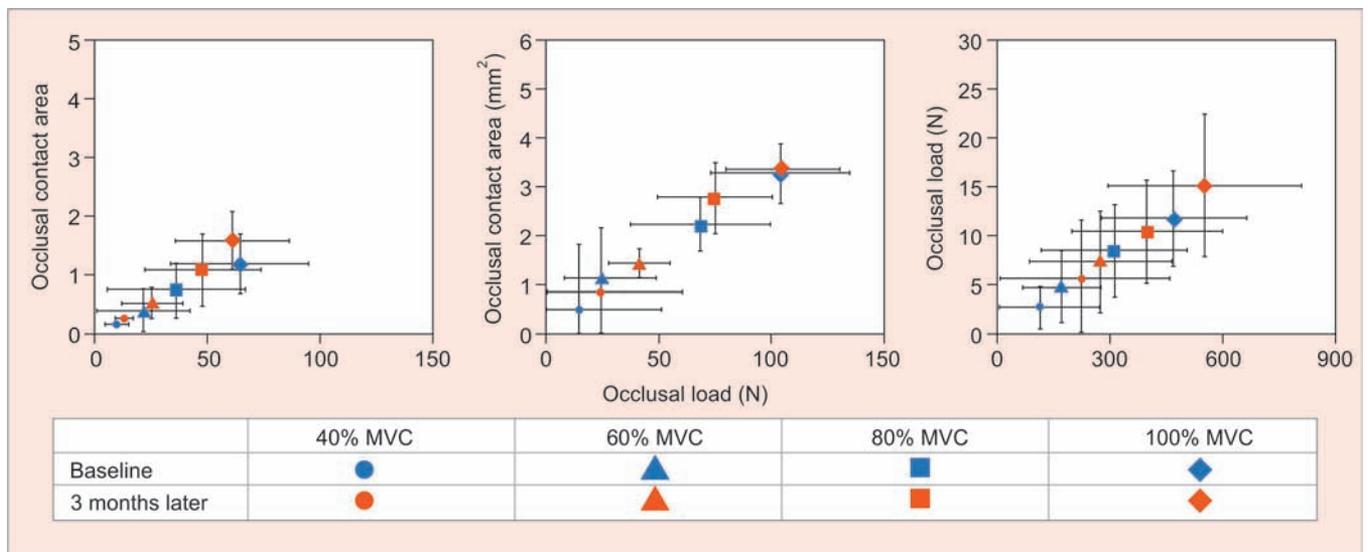
##### Bilateral Molar Region

Occlusal contact area/load remained constant between baseline and 3 months for all clenching strength intensities ( $2.6 \pm 0.1$  and  $2.6 \pm 0.07$  respectively) (Graph 3). No significant differences between baseline and 3-month values were observed at any clenching strength intensity ( $p > 0.05$ ). Two-way ANOVA also revealed no significant difference between baseline and 3-month values ( $p > 0.05$ ). No change in occlusal contact area–load was observed between baseline and 3 months (Graph 6).

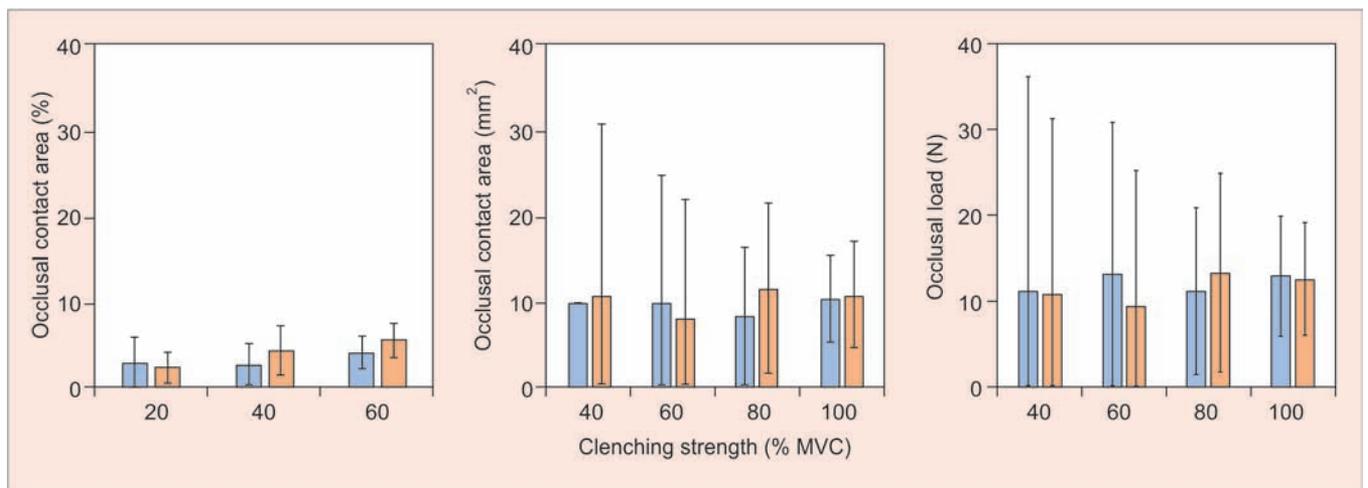
#### Ratio of Occlusal Contact Area and Load of the Prosthesis to the Bilateral Molar Region

##### Ratio of Occlusal Contact Area

We calculated the ratio of occlusal contact area of the prosthesis over the total bilateral molar region (hereinafter, the ratio of contact area of the prosthesis) (Graph 7). No significant difference between the ratio of contact area of the prosthesis was observed between baseline



Graph 6: Relationship between occlusal contact area and load in each region



Graph 7: Time-dependent changes in the ratio of occlusal contact area and load of the prosthesis

and 3-month values ( $p > 0.05$ ). Two-way ANOVA also indicated no significant difference between baseline and 3-month values ( $p > 0.05$ ).

*Ratio of Occlusal Load*

We next calculated the ratio of occlusal load of the prosthesis over the bilateral molar region (hereinafter, the ratio of occlusal load of the prosthesis) (Graph 7). No significant difference in the ratio of contact load of the prosthesis was observed between baseline and 3-month values ( $p > 0.05$ ).

**Ratio of the Contralateral Tooth to the Bilateral Molar Region**

*Ratio of Occlusal Contact Area*

The ratio of occlusal contact area of the contralateral tooth to the bilateral molar region (hereinafter, the ratio of contact area of the contralateral tooth) was determined (Graph 8). No significant change in the ratio of contact

area of the contralateral tooth was observed between baseline and 3-month values ( $p > 0.05$ ).

*Ratio of Occlusal Load*

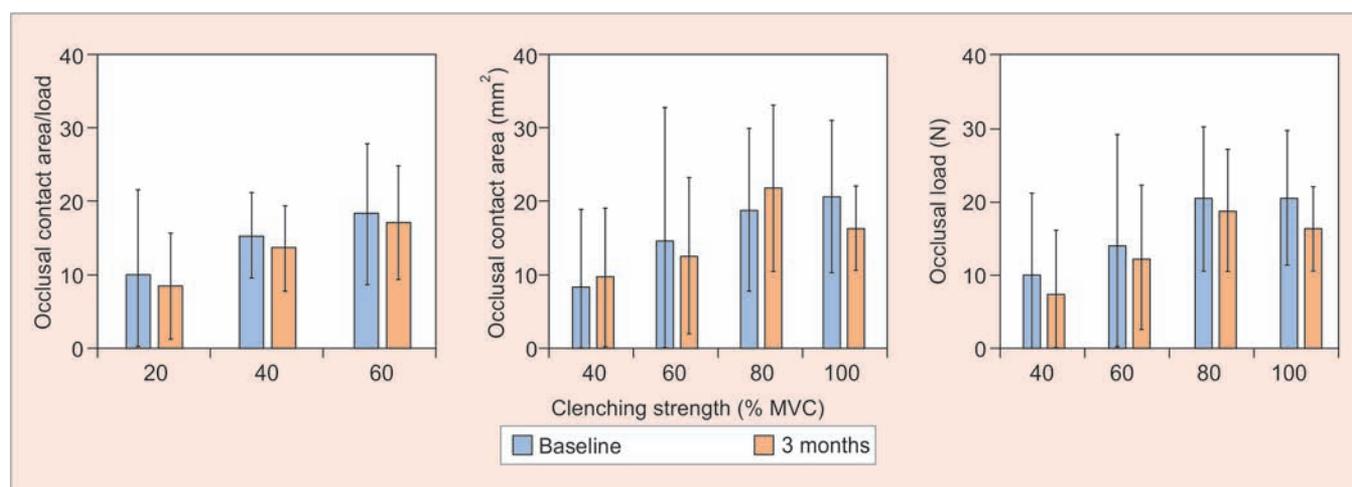
We also determine the ratio of occlusal load of the contralateral tooth to the bilateral molar region (hereinafter, the ratio of contact load of the contralateral tooth) (Graph 8). However, no significant difference was observed ( $p > 0.05$ ).

**DISCUSSION**

**Time-dependent Changes in Occlusal Contact Area of the Prosthesis and the Contralateral tooth**

Okada et al suggested that the amount of change in occlusal contact area of the prosthesis caused by increased clenching strength is smaller than that for the contralateral tooth. We confirmed similar results in this study, finding that the amount of change due to increased clenching





**Graph 8:** Time-dependent changes in the ratio of occlusal contact area and load of the contralateral tooth

strength of occlusal contact area of the prosthesis was smaller than that caused by changes in the clenching strength on the contralateral tooth, both at baseline and 3 months. However, occlusal contact area of the prosthesis at maximum clenching at 3 months and occlusal contact area/load increased significantly, suggesting that occlusal contact area of the prosthesis at maximum clenching had increased. As prostheses do not have shock-absorbing properties, unlike the periodontal membrane of natural teeth, it can be assumed that the shock absorption of occlusal contact during intense clenching is compensated by attrition or inclination of opposing teeth.<sup>14</sup> Furthermore, natural teeth have been shown to extrude over time as occlusal contact is lost. This suggests that in cases where occlusal contact of the prosthesis is set more lightly than remaining natural teeth, extrusion of opposing teeth might occur.

In this study, occlusal contact area and occlusal contact area/load significantly increased between baseline and 3 months when the prosthesis was exposed to maximum clenching. We speculate the increase in occlusal contact area is caused by attrition or extrusion of opposing teeth, and dehiscence of the adjacent contact surface affected the occlusal status of the prosthesis.<sup>14,15</sup>

### Time-dependent Changes in the Prosthesis and Occlusal Load of the Contralateral Tooth

Occlusal load on the first molar of individuals with natural dentition at maximum clenching has been reported to be approximately 130 N.<sup>16</sup> In this study, occlusal load of the prosthesis in the mandibular first molar position was  $63.9 \pm 38.2$  and  $67.5 \pm 44.0$  N at baseline and 3 months respectively. Furthermore, occlusal load was measured at  $103.9 \pm 75.9$  and  $94.7 \pm 66.7$  N at baseline and 3 months respectively, on the contralateral tooth. Occlusal loads at maximum clenching on the prosthesis and the contralateral tooth were also  $<130$  N on the first molar at maximum

clenching in natural dentition individuals at baseline and 3 months. However, considering subjects in the prior study were in their 20s, whereas those in the present study were of middle to old age, the results of our study appear to offer a certain level of validity. As implant-supported prostheses do not have shock-absorbing functions of the periodontal membrane, increased clenching strength is thought to place more occlusal load on prostheses than on natural teeth.<sup>16-18</sup> Maezawa et al<sup>19</sup> suggested that excessive occlusal load may be exerted on the implant-supported prosthesis along with clenching strength even when the occlusal surface is set lower than the occlusal plane. However, we observed that occlusal load placed on prostheses was less likely to increase with greater clenching strength compared with that for the contralateral tooth. This appeared to be due to occlusal equilibration adjustments made by dentists, who took into account pressure displacement during prosthesis fitting by setting a smaller occlusal contact area for the prostheses compared with that for the contralateral tooth.<sup>4,20-22</sup>

When considering the balance between occlusal loads on both sides, ideally, occlusal load of the prosthesis at maximum clenching strength will equal that of the contralateral tooth.<sup>11,23</sup> However, in this study, we found that occlusal load of the prosthesis at clenching strength was smaller than that of the contralateral tooth at baseline and 3 months. Furthermore, there was no significant difference observed between baseline and 3-month values for either the prosthesis or the contralateral tooth. Thus, occlusal loads on the prosthesis and the contralateral tooth remained unchanged between baseline and 3 months.

### Time-dependent Changes in the Ratios of Occlusal Contact Area and Occlusal Load of the Prosthesis and the Contralateral Tooth to the Bilateral Molar Region

The ratio of occlusal load on the prosthesis was approximately 9% after fitting the prosthesis. The ratio of occlusal

load on the contralateral tooth was 15%, indicating that it was larger than that in the prosthesis. There was no change in the ratios of occlusal load on the prosthesis and the contralateral tooth at baseline compared with 3 months, suggesting that the balance of occlusal load on the bilateral molar region remained unchanged over 3 months. The ratio of occlusal contact area of the prosthesis at baseline was approximately 9 and 7% with Prescale and Blue Silicone respectively. Furthermore, at 3 months, there was no significant difference between the ratios of occlusal contact area of the prosthesis and the contralateral tooth. This suggested that there is no change in occlusal load of the molar region or balance of occlusal contact area within 3 months after fitting the prosthesis.

### Analysis of the Total Bilateral Molar Region

Occlusal contact area and occlusal load on the bilateral molar region significantly increased at all clenching strength intensities at 3 months. However, there was no time-dependent difference in the value obtained by dividing occlusal contact area of the bilateral molar area by occlusal load. This suggested that there is no difference in occlusal status of the bilateral molar area between baseline and 3 months.

Based on the results of this study, further investigation including prospective long-term studies is necessary, particularly since prosthesis-related complications and failure are known to occur within 1 year of placement. Future studies should also assess masticatory functions using techniques, such as optical impression to evaluate occlusal form. These studies will help to clarify how the occlusal status of the prosthesis changes in the dentition, as well as demonstrate appropriate recall cycles and occlusal statuses that should be applied in such conditions.

### CONCLUSION

This study suggested that Blue Silicone and Prescale can be used to evaluate time-dependent changes in the occlusal status of prostheses. Our results also suggested that in addition to conventional occluding paper, Prescale and Blue Silicone can be used to quantitatively calculate occlusal load and occlusal contact area.

Although the occlusal status of the prosthesis in the central missing region of the mandibular first molar position did not change over time at weak to medium clenching intensities, occlusal contact area may increase over time at high clenching strength. Furthermore, the finding that both occlusal load and occlusal contact area significantly increased over the total molar region suggested that the maximum clenching strength increased. Accordingly, occlusal contact area and occlusal load of

the bilateral molar region likely increased because the maximum clenching strength increased over the 3-month period after setting of the prosthesis.

### CLINICAL SIGNIFICANCE

This study suggested that implant-supported prostheses which have ideal occlusal contact status need to be checked and occlusal status adjusted regularly for its prediction.

### ACKNOWLEDGMENTS

The authors would like to express their deepest gratitude to the doctors of the Implant Center at Showa University Dental Hospital for their help and cooperation. A partial summary of this study was presented at the 45th Annual Meeting of the Japanese Society of Oral Implantology in Okayama, Japan, in September 2015.

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